TREATMENT STRATEGIES

There are many other treatments listed in the "OPPORTUNISTIC INFECTIONS" section of this workbook. For information about prevention and treatment of Opportunistic Infections, please refer to that section.

Contained in this section is information about TREATMENTS FOR HIV.

THINGS THAT YOU CAN DO THAT ARE AS IMPORTANT AS ANY MEDICATION [1]

1. Reduce stress.
2. Stop smoking
3. Stop all "illicit" drug use whether prescriptions drugs or street drugs.
4. Alcohol in moderation (maximum of 1-2 drinks per day).
5. Safer sex only (even if the other person is HIV+).
6. Eat well - a balanced diet.
7. Vitamin/mineral supplements.
8. Explore complementary therapies.
9. Keep a sense of humor.
10. Learn everything you can about HIV and AIDS.
11. Join a support group. (Avoid "sicker than thou" groups.)
12. Like it or not, you are now a teacher teach the world about AIDS.
13. Allow "negative" feelings - depression, sadness, and anger at times but don't dwell on them.
14. Find a doctor who cares . . . shop around until you are satisfied.

Intervention Against HIV 2

There are several types of intervention which you can take against HIV. All are useful, but no one of them alone is sufficient. Unfortunately, some of these approaches are promoted with religious fervor, to the exclusion of the others. The best overall approach may be one which is inclusive, combining the best of each of the five types of intervention.

1. General Health Maintenance

This means doing all of the things normally recommended for leading a healthy life like proper nutrition and nutritional support; adequate rest; avoidance of alcohol, smoking, drugs and unnecessary stress; exercise and fresh air. Taken alone, good health maintenance won't prevent progression to AIDS or cure it, but it will give each person the best fighting chance he or she has. A good defense against HIV builds upon a solid foundation.

2. Complementary or Supportive Therapies

This category, sometimes called the holistic approach, can include various supplemental supports, such as stress reduction, massage, visualization, yoga and relaxation techniques; psychological and spiritual help natural medicines; and many others. Many of these approaches can be helpful in dealing with symptoms of illness, drug side effects, and keeping one's peace of mind. Taken alone, however, they won't solve the whole problem. Unfortunately, some practitioners of complementary approaches make a dogmatic religion out of them, urging their use to the exclusion of all others, excluding even the medicines recommended by physicians. When presented in this manner, this approach may discourage one from getting necessary medical attention. The best practitioners see these as complementary rather than alternative therapies.

3. Antiviral Strategy

HIV is a virus which attacks and misdirects the immune system. Medicines can help attack the offending virus. The best known antiviral medications are drugs like AZT, ddI, and more recently protease inhibitors. However, there are also some herbal and natural products which have shown antiviral properties, at least in laboratory studies. As such, they too are antiviral medicines and fall in the same general category as AZT, except that they usually haven't been tested scientifically. The challenge of using pharmaceutical drugs like AZT is knowing when and how much to use. The challenge of using herbal and natural products is knowing which ones actually offer real promise in the body. That information is not likely to come from clerks in the stores selling them, but only from trained professionals researching such products. Like other interventions, antiviral drugs alone will not solve all the problems of HIV.

4. Immune Modulating Medicines

The goal of immune modulating medications is to increase the number or function of lost cells, such as CD4 cells, to restore the balance of the various components of the immune system, or to diminish autoimmune activities in which the body attacks its own cells.

Because the immune system is sometimes suppressed, sometimes overactive and sometimes misdirected in HIV it makes sense to seek out medicines which might help correct some of these problems. This is easy to describe but difficult to do. Many researchers feel that we don't yet know enough about the immune system to try to

regulate it with medicines. Some therapies have been shown to influence the immune system in studies, and similar claims have been made about some natural products. There is great popular appeal to the notion that we should help the body naturally regulate itself against HIV. This is a very attractive, common sense sounding approach, but the hard fact is that there is no evidence that anyone really knows how to do this. Moreover, the body's natural defenses almost always seem to fail in the fight against HIV. Perhaps even more than the other types of intervention, it would be unrealistic to expect this approach alone to solve the problems of HIV.

The role of immune modulators in managing HIV disease is still unclear, although increasingly efforts are being made to manipulate the immune system to boost the body's ability to fight disease, suppress potentially harmful immune system activation, and restore immune function. In developing these types of therapies it is difficult to predict the overall effect because of the highly interdependent nature of most immune functions. Improving one area may harm another. At this point, there is no clear or simple strategy for addressing the defects of the immune system in HIV infection.

5. Opportunistic Infection Strategy

Once the immune system has failed to a significant degree, it often becomes necessary to try to prevent the occurrence of the most common opportunistic infections, or prevent their return after a first occurrence.

OI prevention or "prophylaxis" should be considered when CD4 counts are in or nearing a danger zone (for example, the risk of PCP becomes high at a CD4 count of 300 or below, and the risk of CMV and MAC/MAI increase rapidly when the CD4 count falls below 100).

Careful and timely use of medication can prevent PCP altogether. As the incidence of tuberculosis (Tb) rises among some HIV+ people, testing and possibly preventive treatment is recommended. Similar preventative treatment is rapidly becoming available for other infections as well. Using this approach alone, however, would be misguided because it does nothing to slow or stop the decline of the immune system. Even though a person may successfully avoid PCP or MAC/MAI, he or she is still at risk for many other HIV-related infections.

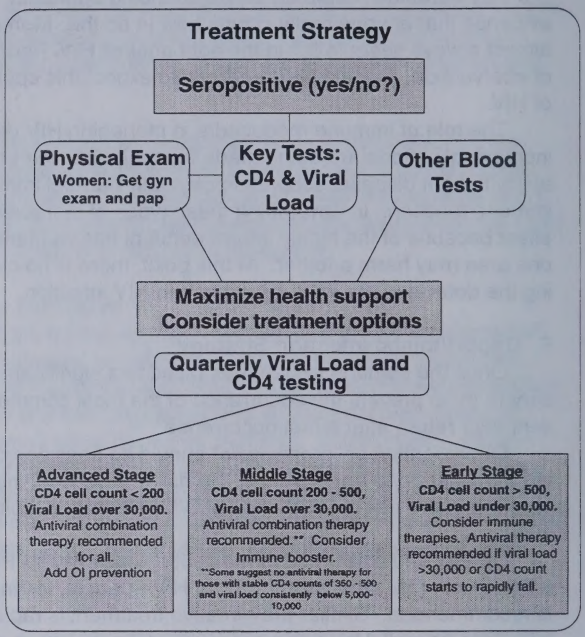
In advanced HIV disease, an infected person often must try to treat or prevent several different opportunistic infections at the same time. This can lead to difficult choices, since many of the medications can interact with each other. Project Inform has three publications which can help sort this out.

(1) The *Project Inform Guide to Opportunistic Infections* (in this workbook in the Opportunistic Infection section).
(2) The *Project Inform Drug Interaction Chart*
(3) The *Project Inform Guide to Gynecological Manifestations and Women's Opportunistic Infections* (in this workbook in the Women's Issues section).

The key to successful intervention is comprehensive inclusion - doing all of the things that makes sense in your individual situation. The biggest mistake we can make is to dogmatically choose one approach over the others. HIV is not a political debate or simple a matter of opinion - it is a life threatening illness. Every decision about treatment has consequences. Each infected person has little room for mistakes. It makes no sense to bet your life on any single philosophy of medicine

Combination Therapy

The last three types of interventions against HIV are usually made with pharmaceutical drugs. Increasingly, researchers agree that HIV will be treated with combinations of these drugs: combinations of one or more antivirals, antivirals plus immune modulators, and both plus any needed treatments for infections. Most studies of antiretrovirals suggest that any one drug used alone has a relatively short period of usefulness. This can be extended by using drugs in rational combinations.


Treatment Strategy
Seropositive (yes/no?)
Physical Exam
Women: Get gyn exam and pap
Key Tests: CD4 & Viral Load
Other Blood Tests
Maximize health support
Consider treatment options
Quarterly Viral Load and CD4 testing
Advanced Stage
CD4 cell count < 200
Viral Load over 30,000.
Antiviral combination therapy recommended for all.
Add OI prevention
Middle Stage
CD4 cell count 200 - 500,
Viral Load over 30,000.
Antiviral combination therapy recommended.** Consider Immune booster.
**Some suggest no antiviral therapy for those with stable CD4 counts of 350 - 500 and viral load consistently below 5,000-10,000
Early Stage
CD4 cell count > 500,
Viral Load under 30,000.
Consider immune therapies. Antiviral therapy recommended if viral load >30,000 or CD4 count starts to rapidly fall.

Discussion: The Debate about when to Start Treatment

The earliest possible treatment is recommended for just about every known illness. There is little reason to think that HIV is any different. In fact, early treatment may be even more important because of the seriousness of the disease.

Starting points for antiviral, immune modulating, and OI medications are the subject of disagreement. Many believe that antiviral medication is appropriate immediately upon learning of the infection whether or not the CD4 count is falling or whether symptoms are evident. Waiting longer might only let the infection progress as it slowly damages more and more T-cells and spreads to other parts of the body. Many researchers believe that viral load tests can help determine when it is appropriate to begin treatment.

Some people feel that, since HIV infection seems dormant for long periods, during which no major visible damage occurs, there may be little point to treating an inactive infection. More recent evidence, however, shows that the virus is always active and that damage to the immune system is always taking place, perhaps at levels too low for current tests to detect. Thus they feel antiviral medication is appropriate at the earliest possible moment, when it can perhaps prevent further spread of the virus. They also note that healthy seropositives have far less trouble with the side effects of such drugs as AZT and ddI.

AZT studies show that treatment at early stages slows progression toward AIDS and that side effects are less severe, or even non-existent in healthier patients. The side effects of AZT are now well known and can be delayed or prevented; the effects of HIV, in contrast, aren't nearly so predictable, manageable or reversible. However, studies of AZT, when used alone, have not sown that using the drug actually helps a person live longer, even though it may slow the decline of the CD4 count. The effects of early treatment with combination therapy look much more promising.

There is no argument about the need to start antivirals when symptoms are present and the CD4 count is falling.

The starting point for using immune modulators may some day be based on T-cell counts (CD4 counts) or measure of CD4 cell function. When the count is sufficiently high there are enough CD4 cells for effective immune response and to continue replenishing the immune system. The natural chemicals which sustain the growth of CD4 cells, called growth factors, are made by the CD4 cells themselves. Thus, when the count falls too low, it is very difficult to get it back up again. In short, you must have an immune system to rebuild one.

CD4 Cell Ranges

Lowest	Low	High
under 200	(200 - 500)	(500 plus)

High Range: In general, a CD4 count above 500 suggests no immediate danger. The 500 level is often cited as the bottom of the "normal" range, but this can be misleading. While an occasional drop to 500 may be normal, a steady or falling count of 500 or even 600 is not normal and indicates suppressed immunity. At the very least, dietary counseling, nutritional supplements, T-cell monitoring and periodic use of other tests are recommended in this range, whether or not treatments are used. With counts this high, many people don't feel motivated to begin treatment. But a growing number of researchers believe it may be the best time to do so -- early therapy *may* have the largest impact against the virus.

Low Range: Studies often exclude people with more than 500 CD4 cells because symptoms are uncommon above this level. Still some AIDS related conditions and even KS can occasionally strike people with CD4 counts above 600. Therefore, as a general guideline, when the CD4 count falls around or below 500 on two consecutive tests, or if it shows a steady decline toward 500 in repeated quarterly tests, antiviral therapy is generally appropriate and enhanced attention to nutritional issues is highly recommended.

Lowest Range: CD4 counts below 200 indicate the greatest risk of infections and according to the 1993 definition of AIDS, a CD4 count of 200 or less constitutes an AIDS diagnosis. It is important to remember that absolute CD4 counts do not necessarily correspond to CD4 cell function. A person with counts below 200 CD4 often remain stable for many years, especially with careful health management. There are exceptions, but even people in this range who seem healthy have greater difficulty combating infections when they occur. While some people have warning signs in the form of symptoms before major infections occur, this is not always the case. Some people progress directly from apparent health to serious OIs.

It has become common to put people with CD4 counts below 200 on preventive treatment against PCP (for example, Bactrim/Septra or dapsone), along with all people who have already had a bout of pneumocystis. Prevention strategies for all of the most common opportunistic infections are described in the Opportunistic Infections section of this workbook. Regardless of CD4 count, yearly monitoring for tuberculosis is becoming increasingly important.

Treatments should only be used under the care of an experienced physician. Patients and physicians are encouraged to enter into collaborative relationships with shared responsibility for achieving and maintaining health. The choice of treatments need not be dictated by either party, and each should strive to understand the other's concerns and requirements if

disagreement arises. Treatment should always be accompanied by monitoring which evaluates the success or failure of treatment. Both patient and physician should be prepared to adjust strategy based on the results of the monitoring process. This model of flexible, monitored treatment used in the context of a collaborative doctor/patient relationship is the key to managing HIV as a chronic illness.

EARLY CARE OF PEOPLE WITH HIV 3

First and foremost, find an experienced and trustworthy physician with whom you feel comfortable managing your health care.

Initial Evaluation

History

Your doctor will ask about any symptoms that may be caused by HIV infection. Be sure to share information about other medical and psychiatric illnesses for which you are treated. Tell your doctor about any medications you are taking. Also, describe any alternative or complimentary therapies you are using.

Physical Examination

Your doctor will do a complete exam looking for signs of HIV disease and opportunistic infections.

Lab Work (Blood work)

1. Baseline Viral Load test

2. CD4 + T cell counts ("T cells ")

3. Complete blood count (CBC)

a. White blood cell count (WBC):
   1. Lymphocytes (T cells and B cells)
   2. Neutrophils (granulocytes)
   (White blood cells are immune cells which help to fight infections)

b. Hemoglobin/hematocrit (HGB/Hct): These are tests of red blood cells which carry oxygen in the blood.

c. Platelets are cells which help to clot blood.

4. Liver Function Tests (LFT's)

a. AST (SGOT), ALT (SGPT), LDH, alkaline phosphatase, and bilirubin are blood tests which tell how well the liver is functioning.

5. Pregnancy Test:

Since many medicines can harm a developing fetus, all women should have a pregnancy test before being treated with drugs to fight HIV.

6 . BUN, Creatinine, and a urine test

Provide information about how well the kidneys are functioning.

Screening Tests

These tests allow your doctor to determine if you harbor infections which can be reactivated when the CD4 counts drops below 200.

Hepatitis B

Since both viruses are transmitted in the same way, many infected with HIV are also infected by hepatitis B. Hepatitis B generally causes a short term clinical illness but in a small percentage chronic liver inflammation can result. Once you are infected with hepatitis B, your blood test will always be positive. The blood test can also determine if you are in the minority who have developed chronic hepatitis. If your blood test indicates that you have never been exposed to hepatitis B, your doctor may recommend a vaccination to prevent a future infection.

Syphilis Test

Since untreated syphilis can involve the brain and cause neurologic (brain and nerve) damage, it is essential to treat syphilis as early as possible. If your blood test shows the presence of syphilis and you have never been treated, your doctor will recommend treatment with penicillin and possibly a lumbar puncture (spinal tap) to look for syphilis in the spinal fluid.

Toxoplasma Antibody

The toxoplasma blood test evaluates if you have ever been exposed to the infection through undercooked meat or contact with cat feces. If the test is positive, there are medications which can help keep the infection in an inactive state.

Cryptococcal Antigen

This blood test evaluates for the current infection with a fungus called cryptococcus.

Other Tests

The following are done as indicated by gender, history, or physical findings.

Pap Smear (Every six months)

This test can detect signs of cervical cancer at an early stage, when it is extremely treatable. Cervical cancer is more common in women with HIV, so pap smears are done every six months.

TB Skin Test

Please see information about Tuberculosis (TB) in the Opportunistic Infections section of this workbook.

Chest X-Ray

A chest x-ray can show signs of tuberculosis. The screening x-ray is done to have a baseline normal x-ray to compare with future x-rays done when you may have symptoms of pulmonary (lung) disease.

T Cell Markers for Treatment:

> 500	Treat symptoms as needed; check T cells every 6 months.
500	Consider antiviral treatment (Thrush, herpes and TB may appear).
200	Consider antiviral treatment, prophylaxis for prevention of OIs (especially PCP), higher risk for opportunistic infections).
100	Opportunistic infections more common.

Which Vaccinations? 4

Recommended Vaccinations:

Pneumovax

This vaccine helps prevent infection with a type of bacterial lung infection called pneumococcus pneumonia. The vaccine is, usually, given once but some physicians recommend one every 5 years.

Influenza Vaccine

The vaccine must be given yearly since the influenza virus varies from year to year. It helps to prevent against influenza virus infection which causes severe "flu" which can be fatal in those with HIV. The vaccine does not offer any protection from the hundreds of viruses which can cause colds. You should always discuss with your physician if the vaccine will do more harm than good when your CD4 count is under 100.

Tetanus Vaccine

This vaccine is given every ten years (this is recommended even for those without HIV).

Hepatitis B Vaccine

This vaccine is given only to those who have never been exposed to hepatitis B.

Vaccinations to Consider:

Hepatitis A Vaccine

Men who have sex with men are at greater risk of contracting Hepatitis A. While rarely fatal, this virus can debilitate. The vaccine is produce from inactivated (killed) strains of the virus, therefore it should not be able to cause you harm. In preliminary studies, no safety issues have been identified in persons with HIV. A large scale safety and immunogenicity is ongoing.

The HIV+ individual needs to protect his or herself by getting certain vaccinations and avoiding others.

Vaccinations to AVOID:

- the oral polio virus, and;
- the MMR vaccine (for measles, mumps and rubella.)

Getting these vaccinations can be dangerous. Rather than protecting against infection, these live virus vaccines can actually cause illness in the immunosuppressed individual. A potentially dangerous situation exists with some university and college vaccination programs instituted on a population with a growing incidence of HIV infection.

Viral Load Basics

The New Test in Town: Viral Load [5]

Unlike CD4 tests that measure the strength of the immune system, viral load tests measure the actual amount of virus present in a person's blood. Using these tests with standard CD4 counts, we are able to get a clearer picture of how effective various anti-HIV treatments are and help map out a strategy for combating opportunistic infections.

Currently, two primary tests exist to measure viral load. One is called a Q-PCR (or sometimes just a PCR) and the other is called a branched DNA (or sometimes a bDNA). Both tests were approved by the FDA this year which should make them more widely available as well as decrease the cost and make insurance reimbursement more likely. It is important, if possible, that once you start with a particular test that you continue to use that test (either the Q-PCR or bDNA). That way you will more easily be able to trend your results.

What Does a Viral Load Test Do?

Both the PCR and the bDNA measure the number of HIV RNA particles per milliliter of blood. The number of RNA particles is known as the viral load or viral burden. Because HIV reproduces through the production of RNA, these tests help us to understand how much of the actual virus is living and reproducing in the body. Studies indicate that, in general, long-term non-progressors tend to have lower viral loads. Following this logic, we can presume that the longer we can keep the viral load low, the longer a person will live and the healthier they will be.

We are only sure that these tests measure the virus in the blood, but we think that they are also a good indication of the amount of virus in the lymph nodes as well. If this is true, then viral load tests will probably become one of our best tools in fighting HIV. These tests measure viral load in terms of copies of RNA. Although it is still debatable as to whether the PCR or bDNA test is more effective, it appears that the PCR is the more sensitive of the two. For the most part, bDNA tests cannot detect viral load lower than 10,000 copies/ml. Likewise, the PCR can detect as little as 250 copies/ml.

Both tests measure changes in viral load in terms of "logs." A log indicates changes in a logarithmic scale. Each log represents a 10-fold change. For example, if your first viral load test indicated 125,000 copies of HIV RNA, and your second viral load test was 12,500, this would be a one log change. If the third test measured 1,250 copies, this would be a two log change. Sustained drops in viral load of three logs is considered a significant change.

Because we are just now beginning to understand how to effectively use viral load tests, we can only provide guesses as to what viral load levels themselves mean. The important thing to remember about viral load tests is that we still need to find out how best to use this information, and therefore it is important to have a thorough discussion with your health care provider before jumping to any conclusions about what the tests mean. It is also important to read up on viral load tests so that you can ask your provider the right questions, and make sure that she or he has the most current information.

Importance of Measuring Viral Load

The International AIDS Society (IAS) panel convened in 1996 agreed that plasma HIV RNA measurements (Viral Load) are important for predicting the risk of clinical progression. It has been demonstrated in clinical trials of combination therapies that reductions in viral load are associated with increased survival and decreased progression to AIDS. The panel did not provide precise viral load points for treatment of specific clinical situations because the data is not yet available to define a single first-line regimen for any given indication.

Viral replication, Viral Load and Disease Progression

Early infection of lymphoid tissue, with continuous high-level viral replication throughout the course of HIV disease is well documented. Half of the virus population in plasma is turned over within hours, which translates to billions of virions produced and destroyed each day. The rate of virus replication stabilizes after primary infection at a particular level or "set-point" in each individual. The set point is strongly associated with rate of disease progression, on a continuum of with risk of progression increasing as the viral load increases. At one extreme of this continuum, a small proportion of individuals with very long-standing HIV infection have low viral loads and near normal CD4 cell counts and appear to have a particularly slow course of disease progression. At the other extreme, those with high viral loads (>50,000 - 100,000 HIV RNA copies per milliliter of plasma are at a greatly increased risk of clinical progression.

Viral load tests provide us with extremely valuable new information, but it is important to remember that the total amount of the virus in the body cannot be directly calculated from the plasma viral RNA level. However, viral load measurements tend to be more predictive of disease progression than CD4 counts. The panel reported on the remarkable agreement between two studies where individuals in the lowest quartile (the 25 percent of subjects with the lowest viral load level: <5,000 HIV RNA copies/ml of plasma) had the lowest risk of clinical progression to AIDS and death. Individuals with viral loads of more than about 30,000 to 50,000 HIV RNA copies/ml (the highest quartile) were at the greatest risk of progression.

How viral load is measured

Viral load and changes in viral load are measured in logs, a kind of short hand for writing very large numbers. For example, a one-log increase or decrease in viral load equals a change of +/- 90 percent, so that a viral load that drops from 100,000 to 10,000 has decreased by one log. Two logs equals +/- 99 percent; three logs equals +/- 99.9 percent; and four logs equals +/- 99.9 percent. Most doctors do not regard changes of less than 0.5 log to be significant; a few regard changes of less than one log as not significant. Changes that are not regarded as significant usually aren't basis for changing a treatment regimen. Remember that changes in viral load typically occur within four weeks of starting or changing therapy.

Recommended Viral Load Use and Handling [6]

Parameter	Recommendations
Plasma HIV RNA level that suggests initiation of treatment **(What viral load markers indicate you should start treatment?)***	• > 5,000 - 10,000 HIV RNA copies/ml and a CD4 count or clinical status suggesting progression • > 30,000 - 50,000 HIV RNA copies/ml regardless of laboratory/clinical status
Target level of plasma HIV RNA after initiation of treatment **(Where you want your viral load to be after you start treatment)**	• Undetectable; <5,000 HIV RNA copies/ml is an acceptable target
Minimal decrease in plasma HIV RNA level indicative of antiretroviral activity **(looks like the treatment is working)**	• >.05 log decrease
Change in plasma HIV RNA level that suggests drug treatment failure **(Your body may no longer be responding as well to this therapy and you might need to consider other treatments)**	• Return toward (or within 0.3 - 0.5 log of pretreatment value
Suggested frequency of plasma HIV RNA measurement **(How often to get a viral load test)**	• At baseline, take two initial measurements 2 to 4 weeks apart • Repeat assessments every 3 to 4 month, in conjunction with the CD4 cell count • Measure at shorter intervals as critical thresholds for decision points are near • Measure 3 or 4 weeks after initiating or changing treatment.

* Information in bold print added by *Operation: Survive!* workbook editor for clarity

Recommended Minimum Standard of Care for HIV Infection [7]

Initial Positive Test Results

- Get CD4 count and viral load (HIV RNA) measurements for baseline (do this twice, 2 - 4 weeks apart).
- If viral load is ≥ 30,000 copies/ml, regardless of CD4 count or clinical status, consider combination therapy with a protease inhibitor.
- Get TB skin test with a control to rule out anergy (if neither react, you'll get covered by the chest x-ray.
- Get a chest x-ray for baseline and repeat every 6 - 12 months throughout infection.
- Get a test for Syphilis (RPR). If positive, seek aggressive treatment with Benzathine Penicillin (Bicillin)
- Get screened for Hepatitis B (HBV). If negative, discuss the option of HBV vaccine with your doctor.
- Women should have a Pap smear every 6 months, minimum.
- Seek dental care for exam and cleaning every 6 months, minimum, and continue throughout.
- Now is the time for you to work on the "bad" habits you've been meaning to address, like smoking.
- Begin weight resistance and aerobic exercise, progressing as tolerated for the entire HIV process.
- Adjust the nutritional content of your diet, increasing protein, and continue supplements too. Continue throughout the HIV process.
- Always wash fruits and vegetables before eating. Bleaching is optional (1 capful bleach in a sink of water).
- Take great care with drinking water or any water that you may swallow (e.g. brushing your teeth). If distilled or properly filtered water isn't available, boil some and let it cool before drinking.

CD4 count greater than 500:	• Medical evaluation with CD4 and viral load profile every 6 months . • If recurrent herpes infections occur, consider prophylaxis with acyclovir (Zovirax). • Women should have a PAP smear every 6 months. • If you are on medications, keep yourself well hydrated with *water.*
CD4 count between 300 - 500:	• Consider antiretroviral therapy with AZT in combination with another nucleoside analog (3TC, ddC, ddI, d4T) and/or protease inhibitors. • Medical monitoring (CBC & viral load) monthly after starting new antiviral therapy with screening labs as needed for drug toxicity and antiviral effectiveness. • CD4 profile every 4 months (maximum). • Carefully monitor yourself for Thrush, Herpes, Shingles, and Skin Rashes and seek aggressive treatment for them. • Aggressively seek diagnostics and treatment for persistent diarrhea. • Men should begin monitoring testosterone levels and supplemental when <400.
CD4 count below 200 or CD4% lower than 19:	• Medical monitoring every 1 - 2 months, CD4 profile and viral load tests every 3 months. • Start prophylaxis for Pneumocystis Pneumonia (PCP) with Bactrim, or like compound, if tolerated. If unable to tolerate sulfa drugs, talk to your doctor about sulfa desensitization. If this is not available or does not work for you, consider Dapsone or Aerosolized Pentamidine for PCP prophylaxis. • Consider fungal prophylaxis with fluconazole (Diflucan), 100 - 200 mg. three times a week and discuss with your doctor. • Women should have a PAP smear every 3 months from this point on.
CD4 count below 100:	• Medical monitoring every month. • Consider Toxoplasmosis prophylaxis with Pyrimethamine (Bactrim offers protection, too). • Begin Mycobacterium Avium Complex (MAC) prophylaxis with Rifabutin, Biaxin or Azithromycin. • Consider CMV prophylaxis with oral Cytovene (ganciclovir). • Monitor weight and aggressively treat weight loss in conjunction with your doctor. Again, aggressively seek diagnostics and treatment for persistent diarrhea.

Treatment Recommendations From San Francisco General Hospital, San Francisco Public Health Department

CD4 Cell Count per mm^3	Viral Load RNA copies /ml	
fewer than 350	any level	two nucleoside analogues plus a protease inhibitor
350 - 500	more than 5,000 - 10,000	two nucleoside analogues plus a protease inhibitor if needed to reduce viral load to less than 10,000 copies/ml
350 - 500	less than 5,000 - 10,000	ddI or d4T** monotherapy or two nucleoside analogs or observation
greater than 500	more than 5,000 - 10,000	ddI or d4T** monotherapy or two nucleoside analogs or observation or participation in clinical trials
greater than 500	less than 5,000 - 10,000	observation or participation in clinical trials

- Another option is to treat all patients until they have a viral load less than 10,000 copies/ml.
- To obtain a baseline viral load, the initial test would be repeated 2 - 4 weeks later.
- Nucleoside analogues include AZT (retrovir), ddI (Videx), ddC (Hivid), d4T (Zerit) , and 3TC (Epivir).
- Recommendations for two nucleoside analogues would include **one** of the following 2 choices; AZT plus either ddI or ddC or 3TC; or d4T plus either ddI or 3TC.
- Approved protease inhibitors include saquinavir (Invirase), ritonavir (Norvir) and indinavir (Crixivan); protease inhibitors in development include nelfinavir (Viracept, made by Agouron Pharmaceuticals) and VX-478 (made by Glaxo Wellcome/Vertex)

•• d4T monotherapy would be an option only after a prior regimen that included AZT.

HIV THERAPY 8

Anti-HIV drugs can be classified in a variety of ways

- agents which interfere with the virus' ability to replicate, such as AZT and ddC and protease inhibitors
- agents which prevent the virus from binding to cells in the body, such as peptide T;
- agents which may selectively target and kill cells which are infected with HIV, such as the experimental drug, GLQ223 (Compound Q);
- agents and preparations which may enhance the bodies ability to mount an immune response to HIV, such as active cellular immunization (therapeutic vaccines).

Therapies to Combat HIV Infection

The following is a listing of the major types of treatments for HIV, which will be expanded upon throughout this section.

I. Antivirals

A. Nucleoside reverse transcriptase inhibitors (AZT, ddC, D4T, 3TC)

B. Non nucleoside reverse transcriptase inhibitors (Nevirapine, Delavirdine)

C. Protease (AKA Proteinase) Inhibitors (Invirase, Crixivan, Ritonavir, Viracept, Vertex)

E. Acyclovir

II. Immune System Therapy

A. Nutrition (Antioxidants)

B. Cytokines (Interleukins, Interferons)

C. Vaccines

III. Gene Therapy

In early stages of development.

IV. Immune Therapy

Immune-based therapies are directed at strengthening the severely damaged immune system and to assist in destroying the virus in HIV infected individuals.

ANTIRETROVIRALS A TO Z ,

Introduction

Once HIV was identified as the cause of AIDS, a major scientific goal has been to stop or slow growth of the virus. This effort has not yet paid off with a perfect or even long-lasting solution, but some meaningful progress has been made. A balanced approach to understanding and making decisions about antiviral therapy must include knowledge of the benefits, risks, and limitations of existing therapies, as well as the prospects for improvements offered by rational combinations and newer drugs.

Considerable controversy and confusion over the use of antiretroviral therapy arose beginning with the IXth International Conference on AIDS in Berlin in 1992, which led many people to inappropriately abandon antiretroviral treatments. While some of the confusion is the result of misinformation and over-extension of the results of studies presented that year, there remains a good deal of uncertainty about when to start and when to switch or combine antiretroviral therapies. Additionally, the failure of existing drugs to remain effective for long periods of time is often misconstrued as meaning the drugs don't work at all.

Rationale: Antiviral Therapy

Despite doubts and frustration raised by the inability of early drugs to produce long-term benefits when used alone, the rationale for antiviral therapy remains strong.

Whether or not HIV infection is directly responsible for all the disruption in the immune systems of people with AIDS, few scientists doubt that HIV replication is the trigger which sets off the cascade of events leading to cell death and tissue destruction. Studies reported in the last few years have shown that HIV is actively reproducing in lymph tissues at all stages of the disease process, including the long initial period in which infected people appear to be healthy.

Recent studies have demonstrated that there is clear relationship between increased levels of HIV and more advanced disease states. As a general rule, the more virus being produced in the body, the more rapidly disease progresses.

The most recent data show that high levels of virus are produced in the lymph tissues, where as many as 25% of the CD4+ cells may be infected. Other new studies demonstrate that there is an aggressive battle waged on a daily basis between HIV and the immune system, a battle in which literally millions of cells and perhaps billions of copies of virus die. In addition to immune dysfunction caused by HIV, the immune system is overwhelmed by the virus' rapid and constant activity.

Early research with antiviral drugs produced useful, though limited, success; for many scientists, this validates the concept and warrants further development.

When a person is first infected, high virus levels develop which are often accompanied by symptoms and decline in number of CD4+ cells. The immune system succeeds in producing a dramatic, but incomplete, drop in virus levels. CD4+ cell counts return to near normal levels. Following this, a person usually regains full health, typically a decade or longer.

Drugs which significantly reduce virus levels in clinical studies almost always cause some degree of rebound in the immune system, as measured by increased CD4+ counts. Conversely, antiviral drugs which fail to reduce levels also generally failed to improve measures of immune health.

In the most recent studies of the new class of drugs, called Protease inhibitors, higher levels of viral suppression have been accompanied by a proportionally larger increase in CD4+ and CD8+ cells.

Considering these points, it makes sense to attempt to slow down or stop the replication of HIV whenever and wherever possible. The so far unmet challenge of antiviral drugs is to develop a drug which produces very large and long-lasting reductions in virus and one which affects virus levels both in the blood and in the lymph nodes. The hope is that such a drug would provide enough help to the body to permit a major restoration of immune health, or at least a greatly lengthened period of stable health and halt the loss of CD4+ cells. Many scientists argue that unless we can bring the virus under control, other efforts at rebuilding immune health will be futile in the long run.

Targets for Antiviral Therapy

HIV belongs to a family of viruses known as retroviruses. After HIV has entered the body, one of its actions is to infect and take control of CD4+ cells, which play an important role in managing the body's defense against disease. When the virus infects the cells, it combines its genetic material with that of the cell, and from that moment onward, the cell and virus are bound together as one. When infected CD4+ cells are activated, the cell literally becomes a factory for producing more virus, which in turn infect additional cells. Fortunately, the infected cell eventually becomes crippled and dies, otherwise a single cell might be capable of producing enough virus to infect every CD4+ cell in the body.

The most common anti-HIV drugs are all called reverse transcriptase inhibitors. Some of these fall into a sub category called nucleoside analogs, and other are called non-nucleoside reverse transcriptase inhibitors (NNRTI). The newer class of drugs called protease inhibitors work at a later stage, after the virus has successfully infected the cell and is attempting to replicate. Other antiviral approaches, which are not yet in clinical testing, will try to inhibit HIV from replicating at different stages of viral replication.

A recently developed approach, called cellular targeting, aims not at the virus itself, but at the chemical activity inside the cell which is necessary for the virus to infect the cell. The only current drug aimed at a cellular target interferes with material in the cell which the virus uses in the step of reverse transcription.

A final category of antiviral drugs is called antisense, an approach in which artificial genetic material is created which is designed to bind with and block the genetic activity of the virus. Antisense compounds can theoretically be made to interfere with almost any step in the viral life cycle.

Guidelines for Antiretroviral Therapy [10]

At the XI International Conference on AIDS in Vancouver in July 1996, the International AIDS Society (a of prominent HIV researchers and physicians) presented new guidelines for "Antiretroviral Therapy for HIV Infection in 1996," which were also published in the July 10, 1996 issue of the *Journal of the American Medical Association (JAMA).* The panel addressed four central questions about antiretroviral therapy: when to start therapy, which types of drugs to use, when to change therapy, and which types of drugs to use when a change in therapy is indicated. These decisions are difficult considering that clinical determinations must be made for the best use of 9 available antiretroviral drugs at a time when long-term studies with clinical endpoints have been completed for only a few possible combinations.

Panel members tried to take into consideration every possible group that may now need anti-HIV treatment or may need it sometime in the future. Thus, the guidelines fall into five broad categories:

1. **Primary Infection:** for those who have recently been infected with HIV
2. **Initial Therapy:** for those who either just learned of their positive HIV status or those who have known their status but have not had any type of therapy
3. **Changing Therapy:** for those who are experiencing treatment failure or toxicity;
4. **Vertical Transmission:** from pregnant women to their fetuses or newborns; and
5. **Postexposure Prophylaxis:** for those who have knowingly been accidentally exposed to HIV—for example, by a needle stick.

The guidelines were published as "Antiretroviral Therapy for HIV Infection in 1996," in the July 10, 1996, issue of the Journal of the American Medical Association (JAMA). Reprints of the article are available from the International AIDS Society-USA, 353 Kearny St., San Francisco, California 94108. This article summarizes the contents of the published guidelines and includes additional, more recent information presented by the panelists at the Vancouver conference.

Primary Infection

Dr. Richman presented the discussion of the panel's recommendations on treatment of primary HIV infection — that is, during the period of four to six weeks that immediately follow exposure to the virus. Of course, only people who know or strongly suspect that they have been infected can be treated at this time. Estimates of the number of HIV-positive individuals who experience actual symptoms of acute infection—fever, fatigue, swollen lymph nodes, headache, sore throat , sore muscles — range from 30 to 60 percent. During this period, the virus is replicating very rapidly, leading to high viral loads — 1,000,000 to 100,000,000 copies per milliliter of plasma.

The great advantage of treating people during primary infection, said Dr. Richman, is that HIV establishes its infection in the body with just one variant, before it has had the chance to mutate into the vast number of variants that eventually lead to resistance to most available anti-HIV drugs. Thus, holding down the virus's ability to replicate at this early stage should limit its ability to mutate and, therefore, its ability to resist treatments. Another reason to treat people during primary HIV infection is to lower what researchers call the viral "set point." This refers to the level of viral load that each individual seems to establish early in HIV infection. Many researchers believe that this set point can predict how quickly

or slowly the individual will progress toward AIDS.

According to Dr. Richman, clinicians have basically **three options for treating primary HIV infection:**

- observation, without drugs, which offers the advantages of low cost and low toxicity;
- limited therapy and relief of symptoms; or
- complete suppression with the most effective combination of antiretrovirals.

The published guidelines recommend: "treatment of primary infection with the most potent combination therapy available.... If enrollment in a clinical trial not possible, a combination of at least two nucleoside analogues is recommended (e.g., zidovudine [AZT] plus didanosine [ddI], zalcitabine [ddC], or lamivudine [3TC]). The addition of a protease inhibitor or an NNRTI (non-nucleoside reverse transcriptase inhibitor) if available, should also be considered. Preliminary investigations of two- and three-drug combinations are under way.

Some patients with primary infection who were treated with AZT for six months showed better CD4 counts and greater reductions in viral load than who were untreated. No one knows how long such treatment should be continued, but the panel recommends at least six months—the period reported on in the only published study of treatment for this population.

Dr. Richman added one serious caution: Doctors need to understand the long-term implications of whichever treatment course they choose. By choosing a particular therapy, a doctor "has started along a path of evolutionary therapy that cannot be retraced." His implication was that, because of the possible patterns of resistance and cross-resistance that will emerge to different drugs, choosing one drug or combination of drugs early in the course of HIV will eliminate the possibility of coming back to that drug or switching to certain others later.

Starting Anti-HIV Therapy

This phase of the presentation in Vancouver was done by Dr. Volberding. Patients for whom these guidelines would be appropriate are those who have gone at least six months after their infection by HIV. Those people living with HIV who should most seriously consider starting antiretroviral therapy, stressed Dr. Volberding, are those in the following groups:

- ✓ all patients who are having HIV-related symptoms;
- ✓ anyone with 500 or fewer CD4 cells (some would say anyone with a CD4 count ranging between 350 and 500) and low viral load; and
- ✓ anyone with more than 500 CD4 cells and a viral load of 30,000-50,000 copies, or with a rapidly falling CD4 count.

Much of the decision making that must be done about anti-HIV treatment at this level involves the use and understanding of viral load measurements and their meaning. According to the published guidelines, **"Earlier initiation of therapy would be expected to result in a more durable response than would be expected in later stages of illness when a broader array of drug-resistant mutants would be expected to be present."** Moreover, earlier treatment is widely thought to prevent or delay damage to the immune system that cannot be reversed.

These recommendations are expected to apply only to individuals who are antiretroviral-naive—that is, who have never used any type of anti-HIV drug. More and more

anti-HIV drugs are becoming available, making the decision about which initial treatment to use that much more difficult. **The panel, as well as most leading HIV clinicians, firmly recommends, however, that therapy should begin with a combination of two or more drugs — with very few exceptions.**

Dr. Volberding observed that most controlled clinical trials that have been reported on to date include AZT. Thus, the first approved antiretroviral continues to play a prominent role in practice as well as in the panel's guidelines. For those who cannot tolerate the drug, or who refuse to take it for whatever reason, other effective initial therapies are still available. As Dr. Volberding pointed out, trials have shown even ddI monotherapy to be very beneficial. And there are other non-AZT dual combinations, for example, d4T plus 3TC or d4T plus ddI.

What impact protease inhibitors will have on which initial therapy to use remains undetermined. Dr. Volberding pointed to the main advantages: more potent effect and the probable delay or prevention of resistance. The guidelines say that, on the one hand, using the most powerful treatment regimen -- two nucleoside analogues and a protease inhibitor -- may be sensible for the reasons Dr. Volberding cited. On the other hand, there is little clinical experience with such a combination either in initial therapy or in early HIV disease. Thus, they recommend that, until more data are available, initial treatment should be limited to one of the regimens indicated in the tables later in this section. Exceptions to this could be made for patients whose HIV progresses after one of the recommended therapies has been started or for those who have a high risk of HIV progression. The latter would include: symptomatic patients, those with low or rapidly falling CD4 counts, and those with high viral loads.

If a doctor and patient together decide that it is appropriate to add a protease inhibitor at this point, Dr. Volberding seemed to favor the use of indinavir (Crixivan). Saquinivir's (Invirase) potency is limited due to its low bioavailability, he said, and patients on ritonavir (Norvir) experience frequent toxicities and more side effects. Studies are now going on to determine whether development of resistance to one protease inhibitor will lead to resistance to one or more of the others. Because these critical studies are not complete, the guidelines caution, "It is important to maintain continuous drug administration at the optimal dosage level with all protease inhibitors, as dose reduction will contribute to the development of resistance to these drugs. When drug toxicity develops, it is generally better to stop the protease inhibitor drug than to reduce its dose."

Continuing, Or Changing, Therapy

Virtually no one would argue that the hard decision making is over once the critical decision about which anti-HIV treatment to begin with has been made. Few, if any, HIV-positive persons will remain on their initial therapy regimen indefinitely —perhaps not even for very long. Regular laboratory work and the patient's own response to the treatment will determine if and when changing therapies is needed. In general, there are three situations that could lead patient and doctor to decide to switch:

1. Treatment Failure

This is signaled by one of several events: an increase in viral load to within 0.3-0.5 log of the level where it was when therapy began or a progressive rise over a previously stable level; decreased CD4 cell count or percentage; or the appearance of symptoms. "Ideally,"

say the published guidelines, "the patient should be monitored frequently enough that the decision to change the regimen can be made before symptomatic disease progression occurs.... Accumulating evidence suggests that earlier decisions to change therapy are more likely to have a significant impact on disease progression."

2. Toxicity, Intolerance, Or Non adherence

All of the approved antiretrovirals have toxic and other undesirable side effects associated with them for some patients. These include, but are not limited to, nausea, headache, lowered white or red blood cell counts, neuropathy, diarrhea. Sometimes these can be so severe that the individual cannot continue to use the particular drug. Some drugs also interact with each other, either decreasing the effectiveness or increasing the toxicity of one or the other. Both of these problems occur more often in persons with more advanced HIV disease. Finally, some people with HIV are unable or unwilling to stick to the dosing and schedule that their medication may require; this is particularly true of some of the protease inhibitors. Taking less than the required dose or frequently skipping doses can do more harm than good.

3. Current Use Of A Sub optimal Treatment Regimen

"Zidovudine (AZT) monotherapy is a sub optimal regimen and treatment should be reevaluated in any patient who is receiving it." As discussed above, there is now general agreement that almost all anti HIV treatment regimens should be with combination therapy.

What to change to? That, of course, is the question on everyone's mind once patient and doctor agree that the current approach is not working as well as it once was. Dr. Hammer, who presented this part of the panel's guidelines, listed seven issues that need to be considered when making such a decision:

- the underlying reason for the change, as discussed above;
- the individual's prior treatment history;
- the options that are available at the time the decision is made;
- the patient's stage of HIV progression;
- any underlying conditions, such as neuropathy;
- other medications that the person is taking and that could interact with any new drugs; and
- cost of the proposed new therapy and any reimbursement issues that the individual's situation could bring up.

With nine antiretroviral drugs now available, and several more likely to be on the market in the next couple of years, switching therapeutic regimens presents both an opportunity and a burden. If a person can no longer tolerate a drug, the new regimen must include drugs that the patient can both tolerate and be willing to take for a prolonged time. If a regimen has failed for a patient, the new treatment should include drugs that are more powerful have different mechanism of action, and are not cross-resistant to drugs that the individual has already used.

With only one non-nucleoside analogue (nevirapine) now available, the role that this class of drugs will play in treatment regimens is not yet clear, said Dr. Hammer. He did advise that a new treatment regimen should include, if possible, two nucleoside analogues to which the patient has not yet been exposed. This advice does not apply to protease inhibitors since studies of those drugs in combination with each other are few in number and not yet complete. For anyone with advanced disease who is using AZT or who has

been on AZT for a long time, Dr. Hammer urged either adding 3TC or a protease inhibitor or switching to another combination of reverse transcriptase inhibitors. The guidelines also warn that, when changing regimens, persons whose first treatment regimen contained a protease inhibitor should change to a regimen containing at least two new drugs. This is because current knowledge of protease resistance issues is too incomplete to make reliable judgments about adding or alternating protease inhibitors.

Dr. Hammer also cautioned that PCP prophylaxis and other essential measures to prevent opportunistic infections should not be stopped even if the CD4 count goes above 300. There have been too many cases of PCP occurring when individuals stopped taking their preventive drugs when their CD4 count went up. No clear explanation of why this happens is yet available.

Finally, the published guidelines briefly address the question of whether antiretroviral therapy should ever be stopped. Because viral load will begin to rise at once when therapy is ended, "efforts should be made to manage drug-related toxicity before all therapy is abandoned." Exceptions might be made for persons with very advanced HIV disease "for whom there are significant toxicity and quality-of-life issues associated with continued antiretroviral therapy."

When to Start Therapy

Status	Recommendation
Symptomatic*	Therapy recommended for all.
Asymptomatic CD4 cell count < 500	Therapy recommended **
Asymptomatic CD4 cell count > 500	Therapy recommended for those with viral load count > 30,000 - 50,000 or rapidly falling CD4 count. Therapy should be considered for those with viral load count of 5,000 - 10,000.

* Symptoms such as recurrent candidiasis; oral hairy leukoplakia; chronic unexplained fever; night sweats; and weight loss.
** Some suggest no therapy for those with stable CD4 cell counts of 350 - 500 and viral load counts consistently below 5,000 - 10,000.

Recommended Initial Therapy for HIV

Nucleoside Regimens

- ☞ **AZT with ddI** or
- ☞ **AZT with ddC** or
- ☞ **AZT with 3TC** or
- ☞ **ddI monotherapy ***

If a Protease Inhibitor is added to any of these nucleoside only regimens, the choice of which protease inhibitors to use should be based primarily on the drug's potency.

* ddI monotherapy may work less well as initial treatment in people with more advanced HIV.

Other treatment regimens that do not contain AZT have not been studied as thoroughly:
ddI with d4T
D4T WITH 3TC
D4T monotherapy

Selected Options for Changing Therapy Due to Treatment Failure

Initial Regimen	Optional New Regimens
AZT*	AZT with ddI ± a protease inhibitor AZT with 3TC ± a protease inhibitor ddI ± a protease inhibitor ddI with d4T ± a protease inhibitor
ddI	AZT with 3TC ± a protease inhibitor AZT with ddI ± a protease inhibitor d4T with a protease inhibitor
AZT with ddI	AZT with 3TC ± a protease inhibitor d4T with a protease inhibitor
AZT with ddC	AZT with 3TC ± a protease inhibitor d4T with a protease inhibitor ddI ± a protease inhibitor
AZT with 3TC	ddI ± a protease inhibitor d4T with a protease inhibitor ddI with d4T 3TC with d4T

*** All people on AZT monotherapy should be reevaluated.**

Selected Options for Changing Therapy Due to Drug Intolerance *

Initial Regimen	
AZT**	ddI ddI with d4T 3TC with d4T d4T
ddI	AZT with 3TC 3TC with d4T d4T with a protease inhibitor
AZT with ddC **Intolerance to AZT**	ddI ddI ± a protease inhibitor ddI with d4T d4T with a protease inhibitor
Intolerance to ddC	AZT with 3TC ± a protease inhibitor
AZT with 3TC	ddI ± a protease inhibitor d4T with a protease inhibitor ddI with d4T

*** For those whose initial regimen contains a protease inhibitor, new regimens should include at least two new drugs chosen from among nucleoside analogues, non-nucleoside analogues, protease inhibitors (one for which there is likely to be little or no cross-resistance to the first protease inhibitor).**

**** a Protease Inhibitor could be added to the nucleoside analogue regimens listed.**

While helpful, guidelines are typically out of date quickly due to the speed of medical advances today.

The principal questions which must be faced by any one making decisions about the use of antiviral therapies include the following:

- ☞ *When should I begin treatment?*
- ☞ *What should I use?*
- ☞ *How will I know if treatment is working?*
- ☞ *When should I change to something else?*

There are no "right" answers to these questions which work for everyone. What is needed is a process for making one's own decisions about how to proceed, a decision which should always be made in concert with a physician.

When Should I Begin Treatment?

Despite the uncertainty any guidelines, a few points are fairly clear. Treatment is almost always recommended for two groups:

- People who have an AIDS diagnosis (either due to major infections or a CD4+ count below 200).
- People experiencing HIV-associated symptoms.

Unfortunately, such recommendations only call for the use of treatment after the principal damage has been done. Such a strategy ultimately cannot prevent decline of CD4+ cells or AIDS. The effect of treatment is most easily seen in this group because people at this stage are suffering the most rapid decline. This does not mean, however, that this is necessarily the best or the only time to begin treatment. It is simply the easiest and least controversial recommendation for researchers to make.

With current available treatment options, logic should indicate the appropriateness of early intervention.

For people with greater than 200 CD4+ cells but no symptoms, other factors might be need to be considered like whether or not therapy is indicated by current viral load tests. Points to remember:

- Evidence of high levels of viral activity, as measured by the PCR test or the bDNA test. Early studies suggest that test levels below 30,000 copies are usually associated with a stable condition. Higher levels suggest more rapid viral replication, which may lead to more rapid disease progression. Further studies may provide clearer information about the meaning associated with specific PCR test results.
- Evidence of rapidly declining CD4+ levels. For some people, a CD4+ count of 300 or 400 is a stable number which is maintained without large changes for many years.

Under this circumstance, a person may feel less urgency about beginning treatment. For some, however, a count of 300 or even 600 is but a brief stopping point on a rapidly declining curve. When several sequential CD4+ counts show a consistent decline (called a trend), a person might feel more urgency about getting on treatment.

As more experience is gained with the new PCR and bDNA tests, it may be possible to make even more specific statements about when to begin. For now, these tests only add to the information which should be considered. One reasonable, common sense assumption may be to use antiviral treatment when tests or symptoms indicate a high or increasing level of viral activity.

What Should I Use?

That depends. Not all people have access to the same treatment options and different people respond differently to individual drugs. The options include: existing approved drugs and combinations, experimental drugs accessed through clinical trials, and other unapproved drugs. **Considering the unsatisfying results of any drug used alone for more than a year, many physicians believe it may be best to use a combination drug approach whenever therapy is used.**

When beginning therapy, one reasonable approach is to begin with the drugs which have been proven in clinical trials. This way, the potential risks and benefits can be more easily weighed, and your physician is more likely to have experience with the drug and its possible side effects. Others who are willing to accept a higher degree of risk may choose to begin with the drugs or combinations which have shown the highest degree of antiviral activity in preliminary tests, even though these may not be as well understood as the more common therapies. Still others may make choices based on the anticipated side effect profile of the drugs chosen, avoiding any drugs which might have side effects similar to complications the person is already experiencing. For example, a person who has a generally low white blood cell count might avoid drugs like AZT which can further lower the white count. In addition to starting antiviral therapy, nutritional and psychosocial issues should also be considered.

How Will I Know If Treatment is Working?

The indications of a treatment effect vary somewhat depending on the stage of the disease. For people with advanced disease and symptoms, an improvement in symptoms and clinical signs, such as gaining weight, are obvious markers of a response to a drug. In contrast, for asymptomatic people, there are no obvious symptoms to monitor. In this group, changes in lab markers, such as CD4+ counts and viral load are the primary indicators of drug activity.

The most direct indicator of an antiviral drug effect should be a reduction in the level of virus. This can be best measured by the PCR and bDNA tests.

A secondary, indirect marker of antiviral drug benefits has been an increase in CD4+ cells, as measured by the standard CD4+ test. Remember though, that no single CD4+ test by itself should be the basis for making decisions. Instead, the longer-term trend is what matters.

If a drug fails to reduce virus levels, fails to improve CD4+ counts, or both, it is likely to be failing overall. Failure to "fix" certain symptoms, however, is a less clear marker, since some of the symptoms of advanced HIV disease are driven by other infections and not HIV itself.

Regular monitoring of lab tests and clinical conditions should be conducted by a physician,

both to measure drug effectiveness and to watch for drug toxicity. Even drugs which produce an initial positive benefit will almost certainly lose effectiveness over time, and may also produce cumulative side effects.

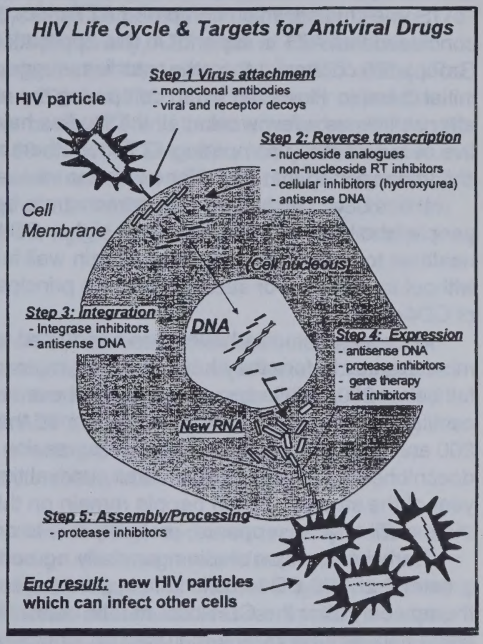
When Is It Time to Change Treatment?

The answer to this question is almost identical to that of the previous question. Any treatment use should be carefully monitored for evidence of both effectiveness and possible side effects. Following trends, in laboratory and clinical findings, is a useful tool in monitoring the disease. Some physicians believe it is appropriate to change treatments when the laboratory evidence, such as viral load tests or CD4+ counts, shows that a person has declined to levels equal to or "below" those found when beginning treatment. Some physicians prefer to wait for the appearance of returned or new symptoms, while others take a more preventive approach and prefer to respond immediately to significant declines in lab test values, in hopes of forestalling clinical decline.

Specific Antiviral Drugs

I. Nucleoside Analogs: Reverse Transcriptase Inhibitors and Related Drugs:

Nucleoside analog drugs interfere with the "reverse transcription" (RT) process by inserting false building blocks or decoys which the virus mistakenly uses when it tries to build "reversed" copy of itself, the first step in making new virus. If the virus takes up the decoy instead of the real material it needs, the process fails, stopping the cycle of the virus before it can take over the core of a cell and thus preventing replication.



Nucleoside analog drugs were the first to be tried against HIV because they were better understood and better proven than other antiviral approaches. Also, at least one of the nucleoside analogs, AZT, has been effective in crossing the blood brain barrier and has been shown to be helpful in managing HIV-related dementia in some persons. Most other antivirals have a very difficult time crossing into the brain.

Although the nucleoside analogs appear to impair HIV's ability to replicate, they are not a cure since these drugs do not totally eradicate the virus from the body. Over time, the virus often mutates or changes itself enough so that it is no longer affected by these drugs. This process, called the development of viral resistance, is likely to happen with almost all antivirals to some degree.

Here is a summary on currently available nucleoside analogs.

AZT (Known as Zidovudine and Retrovir)

AZT is the most widely used, the oldest, and the best known of all the antiretrovirals. It is thus the standard against which new treatments are compared.

What Does the Research Show?

The benefit of AZT therapy, used as a single drug, has been most clearly demonstrated in people with AIDS or who have symptomatic disease and are beginning therapy for the first time. In this group, AZT has been shown to modestly increase survival and reduce the number and severity of opportunistic infections. This benefit fades for some people in as little as six months, but has been shown to extend as long as 21 months for others.

In people who have lowered CD4+ counts and some symptoms but not clinical AIDS

the most clear benefit from AZT has been to lengthen the time before an AIDS diagnosis and to delay the loss of CD4+ cells. In this group, AZT monotherapy does not necessarily increase survival time, most likely because the virus quickly be comes resistant to the drug.

Some persons have demonstrated resistance to AZT very quickly, while others have benefited for longer than two years. Generally, people with higher CD4+ levels develop resistance to antiretroviral therapies less rapidly than people with fewer CD4+ cells.

Some studies which compared AZT monotherapy directly to ddI, as initial therapy, concluded that AZT is superior in this application. Results from ACTG (AIDS Clinical trial Group) 175 contradict the other studies, suggesting that ddI is more beneficial than AZT as initial therapy. However, when comparing the effects of staying on AZT or switching to ddI after as little as a few weeks, all the studies have concluded that switching was more effective. A recent study comparing AZT monotherapy, ddI monotherapy, and AZT plus ddI in children reported that AZT alone was the weakest therapy regimen.

It has been more difficult to demonstrate benefits from using AZT monotherapy in people who have no symptoms and higher CD4+ counts, largely because such people are healthier to begin with and many remain well for the duration of a typical study with or without treatment. For such people, the principal benefit of AZT may be to slow the decline of CD4+ cells.

Four major studies have been conducted testing the value of giving people AZT monotherapy before they have shown symptoms of disease and before their CD4+ counts fall below 200. While some aspects of these studies are contradictory, others aspects are consistent. All such studies have confirmed that giving the drug to people with between 200 and 500 CD4+ cells can delay progression to AIDS for some people, even though this doesn't necessarily lengthen overall survival time. The effect shows up mostly in the first year of the studies. When people remain on this same therapy for longer than one year, the benefit often disappears, probably due to drug resistance.

Early intervention studies generally agree that giving AZT monotherapy to people with greater than 500 CD4+ cells fails to produce any obvious benefit compared to beginning therapy only after the CD4+ count falls below 500. One theory is that using the drug at this stage causes its activity to be used up long before most people in such a study are in any danger of experiencing major disease progression, opportunistic infections, or death. Drug resistance would occur for most people well before critical stages of disease progression were reached.

This finding doesn't mean that earlier intervention against HIV is useless. Instead, it says only that using AZT as long-term monotherapy doesn't work, largely because its period of effectiveness is used up too quickly to make much of a difference. Many researchers are continuing to test other strategies employing combinations of drugs and different types of drugs, in early intervention in hopes of stalling disease progression for long periods of time.

A second conclusive benefit demonstrated by AZT is a reduction in AIDS-related dementia. AZT's impact on dementia appears to be superior to that of most other antiviral drugs, perhaps because it does a better job of crossing the blood brain barrier.

A third clear benefit noted for AZT is that a short-term cycle of use during pregnancy can significantly reduce rate of mother to child transmission of HIV. The study which established this found that giving the drug to the mother in the late stages of pregnancy and delivery, accompanied by treating the newborn for six weeks, resulted in a 2/3 reduction in the number of babies born with productive HIV infection (actually HIV-positive, as opposed to

just showing the mother's antibodies). This is the first evidence that treatment with an antiviral can play a role in preventing transmission of HIV.

The benefits of using AZT in combination with other antivirals have not yet been fully studied, although some benefit was shown in studies which combined AZT with ddC or ddI or 3TC. One recently released study, ACTG 175 indicated that people who had never taken a AZT are significantly more likely to maintain stable CD4 counts and delay progression if they begin therapy with AZT + ddC rather than beginning with AZT alone. ACTG 175 also indicated that for those who had taken AZT previously, AZT + ddI or ddI alone could delay drops in CD4 counts and delay progression better than remaining on AZT alone. The trial looked at people with CD4 counts between 200 and 500. A second study called the Delta trial included both people who had never taken AZT and those who had used it for at least three months, all of whom had between 50 and 350 CD4 cells. Many other studies are currently underway, testing 2 and 3 drug combinations of AZT with other nucleoside analogues, non-nucleoside analogues, and protease inhibitors. Preliminary reports show good results with little added toxicity. Finding the right combination remains a critically important challenge.

What About Side Effects?

The most commonly observed side effects of AZT are headaches, nausea, hypertension and a general sense of feeling queasy. More serious side effects include anemia and suppressed white blood cell counts, both probably due to bone marrow toxicity, and muscle wasting (myopathy). The more serious side effects associated with AZT are generally reversible by lowering the dose or discontinuing use, or managing side effects with supportive therapies, such as erythropoietin (EPO) for anemia and granulocyte colony stimulating factor (G-CSF) for bone marrow suppression.

Side effects of AZT correlate closely with disease stage and dose. In early studies at high doses (1000 to 1500 mg./day) side effects occurred much more frequently than in subsequent studies of lower doses. Additionally, the frequency and severity of side effects associated with AZT are greater in people with more advanced disease. In early disease, the rate of people experiencing serious side effects in studies is relatively low and only slightly different from placebo. Despite these generalizations, some healthy people experience serious toxic effects, while some people with advanced disease easily tolerate the drug. Some people cannot tolerate the drug for more than a few weeks, while others have used it successfully for many years. There is as yet no way to predict who will or will not experience side effects.

AZT sometimes causes temporary problems in the first weeks of use, causing some people to discontinue the drug prematurely. These initial effects include nausea, headaches, hypertension, and a general sense of feeling ill. These effects may be due to the drug itself and/or to the patient's anxiety about taking it.

One difficulty measuring the side effects of AZT is that many of them, such as anemia, bone marrow suppression, and muscle wasting, can be direct effects of HIV disease, unrelated to AZT use.

How to Use It, Dosing and Drug Interactions

Many of the early studies of AZT used doses two and three times higher than those employed today. The general consensus is that such higher doses did not add to the drugs' benefit, but did add to its toxicity. AZT is available in 100 mg. gelatin capsules and an oral syrup formulation for pediatric use. The recommended dose for adults is 500 to 600 mg./

day. The current recommended dosage for children is 180 mg. per meter squared every six hours.

Because AZT is primarily excreted through the kidneys, concurrent use of drugs which have kidney toxicity or which suppress red or white blood cells may increase the risk of side effects from AZT. Concurrent use of such drugs are not necessarily discouraged but should be carefully monitored.

AZT is metabolized through the liver, therefore persons with a history of liver problems should monitor liver function carefully while on AZT. Persons with a history of injection drug use who are currently on drug therapy programs should be aware that morphine and other associated drugs such as methadone are also metabolized through the liver. Some studies suggest that concomitant use of methadone and AZT results in an under-dosing of methadone.

Where to Get It

AZT is an approved drug and can be obtained with a prescription from a hospital or pharmacy. AZT is also usually available through state AIDS drug assistance programs. Additionally, Glaxo Wellcome has a temporary Assistance Program for people who are "medically indigent." For more information on this program call (800) 722-9294, extension 3633.

For more detailed information about AZT, please visit or call the AIDS Survival Project Treatment Resource Center (404) 874-7926.

ddI (known as didanosine and Videx)

ddI, like AZT, is a nucleoside analog reverse transcriptase inhibitor. While ddI works by a similar mechanism to AZT, it has a different toxicity profile and persons who cannot tolerate AZT sometimes are better able to tolerate ddI.

What Does the Research Show?

The best proven value of ddI is its use in people who have previously used AZT therapy at least 12 weeks. When given to people with fewer than 300 CD4+ cells who have already been on AZT for 12 weeks or longer, switching to ddI or AZT + ddI seemed to result in slower decline in CD4 counts, fewer and less severe opportunistic infections, and a longer period before progression, compared to people who simply remained on AZT. People who had previously used AZT for between 8 and 16 weeks seemed to do equally well on AZT or ddI. Some studies suggest that people who use ddI as an initial therapy do less well than those who begin with AZT, however ACTG 175 indicates that ddI is better for initial therapy than AZT.

One study which compared ddI to ddC as a follow-up treatments after AZT or as alternatives for people who could not tolerate AZT showed that both drugs were about eventually effective. However, ACTG 175 and the delta trials, two larger studies, indicated that ddI or ddI + AZT is a slightly better follow-up treatment than ddC + AZT for people who have used AZT.

Many of these studies were able to only show a trend toward prolonged survival for people switching to ddI, though these statistically inconclusive results may be due to the small size of the studies, or the possibility that any increase in survival time really is small.

Several major studies are underway testing ddI in combination therapy. Some of these studies include combination with other nucleoside drugs like AZT, non-nucleoside analogs like nevirapine, protease inhibitors, and drugs which inhibit cellular factors, like hydroxyurea.

Initial data suggests that combining ddI with AZT increases antiviral action, but does not necessarily delay the development of drug resistance.

What About Side Effects?

The most common side effects of ddI are increased uric acid levels, headaches, diarrhea and insomnia. Anemia, the most common side effect of AZT, has not been observed in people taking ddI.

A more serious side effect of ddI is nerve damage called peripheral neuropathy, typically characterized by sharp burning pain sensations in the feet, legs, and/or hands. Irreversible neuropathy has been documented in people taking very high doses of ddI (750 mg./day). Incidence of peripheral neuropathy associated with ddI use appears to be less in people taking lower standard doses (500 mg./day). Early signs of peripheral neuropathy include a tingling sensation in the fingertips, feet and legs, or numbness recurring in the same spots. Others report experiencing a deep pain in the hands and/or feet. This nerve damage heals over time, if caught early, and if use of the drug is discontinued. However, it is recommended that therapy be resumed at half the previously taken dose after neuropathy stops.

Another serious side effect is pancreatitis, which can be fatal, and is sometimes characterized by a sharp pain in the upper abdomen and nausea and vomiting. People who believe they are experiencing symptoms of pancreatitis should discontinue ddI immediately and see their physician. Some physicians monitor amylase and lipase levels, a blood test which measures enzymes which are indicative of pancreatic function. However, amylase and lipase levels may not begin to rise until after pancreatitis has commenced and thus may be unreliable in predicting ddI-related pancreatitis. Incidence of pancreatitis seem to increase when higher doses of ddI are used as well as in advanced stages of disease.

How to Use it, Dosing and Drug Interactions.

ddI is available in three different formulations: tablets, buffered powder for oral solutions and pediatric powder for oral solution. The tablets are currently the standard formulation. The recommended dose depends on body weight. For adults weighing less than 60 kg. (132 lb..), the starting dose is 125 mg. twice daily: and for those weighing more than 60 kg., 200 mg. twice daily.

Because ddI cannot be absorbed in an acidic stomach environment, a chemical buffer has been added to the tablets. To get the correct buffering, <u>two tablets must be taken together</u>. If the dose needs to be reduced, different dose tablets need to be used as there will not be sufficient buffer on only half of a two tablet dose. Doses should be taken every 12 hours, on an empty stomach, as food can reduce the absorption by as much as 50%.

Because ddI is administered with a buffer to reduce stomach acidity, drugs which require an acidic environment in order to be absorbed, such as dapsone, cimetidine, ranitidine, and ketoconazole, should not be taken within two hours of ddI. Additionally, quinolone antibiotics such as ciprofloxacin, should not be taken within two hours of ddI as the buffer can reduce the absorption of some quinolones. Also ddI should not be administered with a prescription antibiotic containing any form of tetracycline.

Combining ddI with oral ganciclovir or IV pentamidine may increase the risk of pancreatitis. Alcohol use while taking ddI can also increase the risk for pancreatitis. Additionally, ddI doses may need to be adjusted for people with kidney or liver impairment. ddI should not be used in combination with ddC as the risk of developing peripheral neuropathy and pancreatitis increases

Where To Get It

ddI is an approved drug and can be obtained with a prescription from a hospital or pharmacy. ddI is also usually available through state AIDS drug assistance programs. Additionally, Bristol-Meyers Squibb has a help line to assist people with insurance payers' policies and procedures, and they will help people in identifying alternative reimbursement sources. A temporary assistance program has also been established to provide ddI free of charge if medical and financial criteria are met. For more information on this program, call (800) 788-0123.

For more detailed information about ddI, please visit or call the AIDS Survival Project Treatment Resource Center (404) 874-7926.

ddC (known as zalcitabine or Hivid)

While ddC works by a mechanism similar to AZT, it has a different toxicity profile and people who cannot tolerate the side effects of AZT might better tolerate ddC. In this regard, ddC is often seen as an alternative equivalent to ddI, although there are some possibly important differences between the drugs.

What Does the Research Show?

When ddC was used as an initial treatment and compared to AZT, people receiving ddC fared less well than those receiving AZT. ACTG 175 recently indicated that a combination of AZT + ddC is a better initial therapy than AZT alone. Studies comparing ddC to ddI as follow-up treatment to AZT or as alternatives in people who could not take AZT found ddC to be roughly equivalent to ddI, though some trials suggest ddI or ddI + AZT is a be therapy than ddC + AZT for those who have already used AZT. Since ddC and ddI have not been studied in precisely the same fashion, it is difficult to compare their value, either individually or as alternatives to AZT.

Perhaps because ddC is a highly potent compound compared to its weight, studies of the effectiveness and safety of ddC have shown that using accurate and proper dosing of ddC is important, more so than with other drugs. Taking a small amount less than recommended quickly renders the drug ineffective, while taking small amounts more than recommended can quickly produce unnecessary side effects.

The first large study of combination therapies compared ddC plus AZT to ddC alone and AZT alone. Because of the wide range of volunteers in the study, ranging from zero CD4+ cells to 300 CD4+ cells, the overall study results showed no significant differences between the three drug regimens. More careful analysis of the results, however, showed that people with the fewest CD4+ cells (less than 150) did not benefit from combination therapy and may have experienced greater side effects from the combination. In contrast, people with CD4+ counts above 150 experienced the best results from the combination of ddC plus AZT. The Delta trial, conducted in Europe and Australia, essentially supports this data for people who have previously used AZT, but showed a clear benefit to using a combination of either AZT + ddC or AZT + ddI for those who have never used AZT. Further analysis of the results of Delta and ACTG 175 may clarify these results. Many additional studies employing ddC in combination with other therapies are underway.

What About Side Effects?

ddC has a number of side effects which are usually temporary and typically resolve

within two weeks of initiating therapy, these include rashes, chest pain, fever, nausea, elevated liver enzymes and mouth sores.

Because ddC is eliminated through the kidneys, persons with kidney impairment should consult with their physicians about appropriate use of this drug. In one study of seven participants with kidney dysfunction, the half-life of ddC was four times longer than in persons with normal kidney function. The levels of ddC in blood was also higher for some of these participants with kidney dysfunction. Creatinine clearance should be monitored to evaluate ddC clearance and dose should be reduced to avoid ddC toxicity if there are any abnormalities. Additionally, ddC use may worsen preexisting liver problems.

The most serious side effects of ddC include dose-related nerve damage, known as peripheral neuropathy (see ddI side effects). As with ddI, the incidence of peripheral neuropathy use appears to be less in people taking lower doses of the drug. ddC induced neuropathy can be exacerbated with use of ddI. Persons who discontinue use of ddC because of neuropathy should exercise caution in using ddI as the effect of nerve damage with these drugs are additive.

Another serious side effect of ddC is pancreatitis (see ddI side effects), which has been fatal in some people. Pancreatitis is characterized by a sharp pain in the upper abdomen and nausea and vomiting. People who believe they are experiencing symptoms of pancreatitis should discontinue use of ddC immediately and see their physician. Incidence of pancreatitis seem to correlate with higher doses of ddC and further advanced stages of disease. In controlled studies and the expanded access program, less than 1% of the participants receiving ddC developed pancreatitis. As ddI can also cause pancreatitis and peripheral neuropathy, ddI and ddC should not be used in combination.

Other serious side effects of ddC include esophageal ulcers and congestive heart failure. Incidence of these events are extremely rare. A preexisting heart problem may be made worse by use of antiretroviral therapy and there needs to be careful monitoring.

How to Use It, Dosing and Drug Interactions.

ddC is available in tablet formulation. The optimum dose of the drug appears to be 0.75 mg. 3x/day. Although weight seems to be an important variable, dose adjustments do not need to be made in persons falling between 50-100 kg. Studies have shown that ddC should be taken on an empty stomach as the absorption of ddC was decreased when taken with food.

Because of the danger of pancreatitis, combination of ddC with other drugs which may cause pancreas toxicity, such as ddI, intravenous pentamidine and ganciclovir, need to be carefully monitored. Additionally, alcohol use can also increase the risk of pancreatitis.

Drugs such as amphotericin B and foscarnet may increase the risk of peripheral neuropathy or other ddC related toxicity by interfering with the elimination of ddC through the kidneys. Drugs associated with the development of peripheral neuropathy, such as dapsone, should be used with caution.

Where to Get It

ddC is an approved drug and is widely available with a prescription through hospitals and pharmacies. ddC is also usually available through state AIDS drug assistance programs. Additionally, Hoffman-LaRouche has set up a hotline to give health care providers information on how to use ddC as well as reimbursement options. An indigent patient program will provide ddC free of charge to persons who cannot identify other reimbursement sources. For more information call (800) 285-4484.

d4T (known as stavudine and Zerit)

d4T is another nucleoside analog reverse transcriptase inhibitor. There is less information available about how to best use this drug compared to the other approved antiretroviral therapies. However, the completion of recent studies prove that the drug has a useful place in the treatment of HIV disease.

What Does the Research Show?

Studies of d4T have thus far been limited. The drug was approved for use when an early analysis of an ongoing study showed that, in people who had previously used AZT for at least 24 weeks, switching to d4T produced greater benefits and lesser toxicity than remaining on AZT. The benefits of d4T seen in the initial analysis included improved CD4+ cell levels, reduced virus levels, improved weight gain, and subjective health compared to people who remained on AZT treatment. This study evaluated d4T in people with between 50 and 500 CD4+ cells. Final data from the completed study have confirmed that the early analysis was a reliable predictor of long-term outcome. In the final analysis, patients who were switched to d4T experienced a delay in disease progression when measured either by surrogate markers, such as CD4+ cell levels, or by clinical outcomes, such as time before the development of opportunistic infections. These findings were confirmed in volunteers who entered the study at any of three different stages of disease progression. The d4T treated group sustained a significant increase in CD4+ cell levels, averaging 40 points, throughout the duration of the trial. There was also a strong trend toward increased survival in the d4T treated group, a finding which almost, but not quite, reached the level of statistical significance.

There are still many questions regarding the appropriate use of d4T, including: how d4T compares to AZT (or combinations) as initial treatment; when to switch to d4T from other antiretroviral therapies, what is the best dose, what are the potential drug interactions, how quickly resistance to d4T develops and how to use this drug in combination with other antiretrovirals.

What About Side Effects?

The major side effect that has been reported to date has been peripheral neuropathy (15-21% of participants in clinical studies). In most cases, the symptoms were resolved after the drug was withdrawn or given at a lower dose. Other side effects include increases in liver enzymes and neurological complications (this has been more commonly reported in community surveys of people taking d4T than reported in clinical studies).

Pancreatitis has been reported in about 1% of people taking d4T, the same level seen in people receiving AZT. Pancreatitis is not considered to be a side effect of AZT. Thus, it is still not known whether prolonged use of d4T or use of d4T in combination with other therapies may increase the risk of developing pancreatitis.

People with a history of liver problems should monitor their liver function tests closely. Although no formal drug interaction studies have been done, caution should be exercised in taking d4T at the same time as taking other drugs or therapies which impair liver function.

d4T seems to cause a modest degree of bone marrow suppression, but the incidence is low compared to AZT.

How to Use it, Dosing and Drug Interactions.

The dose of d4T used in clinical studies has been 40 mg. twice a day without regard to meals. The Parallel Track program showed that a 20 mg. twice a day dose was as effective

as the 40 mg. twice a day dose and there was significantly less peripheral neuropathy.

Drug interaction studies are still underway, but there are a few drugs which also have side effects of peripheral neuropathy which should be used with caution in combination with d4T. Drugs such as amphotericin B and foscarnet may increase the risk of developing peripheral neuropathy. Dapsone, which is also associated with the development of neuropathy should be used with caution. Ganciclovir and intravenous pentamidine may increase the risk of pancreatitis.

Where To Get It

d4T is an approved drug and is available with a prescription through hospitals and pharmacies. d4T is also usually available through state AIDS drug assistance programs. Additionally, Bristol-Myers Squibb has established a patient assistance program for people who do not have private insurance or other sources of reimbursement. For more information, call (800) 788-0123.

For more detailed information about d4T, please visit or call the AIDS Survival Project Treatment Resource Center (404) 874-7926.

3TC (also known as lamivudine or Epivir)

The most important other nucleoside analog reverse transcriptase inhibitor in advanced clinical testing is 3TC.

Data from two European studies of 3TC in combination with AZT show encouraging results. These data have recently been confirmed by two similar studies conducted in the US. Taken together in combination, these studies suggest that combining 3TC with AZT results in longer sustained suppression of HIV, and a longer period of improved CD4+ cell counts. These initial data seem superior to those seen so far for any other reported combination of reverse transcriptase inhibiting drugs. Researchers believe this may be due to the fact, observed in the laboratory, that resistance to 3TC will make the virus susceptible to AZT. How these results will compare to studies which include protease inhibitors is not yet known, but many researchers are very interested in the addition of a protease inhibitor to the AZT plus 3TC combination.

When used as a single agent, 3TC does not appear to be very effective. The virus develops resistance very rapidly and any possible initial benefit is quickly lost. Data suggest that 3TC should only be used as part of a combination with AZT. It's value in combination with other treatments, such as d4T, ddI, or ddC is unknown.

Where To Get It

3TC is an approved drug and is available through prescription and many state assistance programs. Glaxo Wellcome has established their own assistance program, which can be reached at (800) 513-3028.

For more detailed information about 3TC, please visit or call the AIDS Survival Project Treatment Resource Center (404) 874-7926.

Nucleoside Analog Drug Resistance

Much information regarding AZT resistance has come out of a study comparing AZT and ddI. This study showed that people who entered the trial with high level of AZT resistance progressed significantly faster than people without it. People who were resistant to AZT and then switched to ddI received no clear benefit from switching therapy. People who switched to ddI before developing AZT resistance progressed less rapidly than those who continued on

AZT. This suggests that it may be important to know when drug resistance is beginning, so that people may be able to switch therapies while they can best benefit from doing so.

Test tube studies show some degree of cross resistance between AZT and some of the other nucleoside analogs - d4T and ddC. If this holds true in human use, people who have developed resistance to AZT may also see diminished benefit from drugs which show cross resistance. There is no cross resistance between AZT and ddI or 3TC, so this may make a good choice for follow-up after AZT use or in combination with AZT. In test tube studies, 3TC is able to cause viral mutations which make AZT-resistant virus sensitive to AZT again. Studies are now ongoing to see if this occurs in humans.

Resistance to ddI is well documented in test tube studies. It appears that ddI resistance develops less rapidly than AZT resistance, though this does not necessarily mean that ddI works for a longer period than AZT. There is considerable cross resistance between ddI and ddC. There may be some cross resistance between ddI/ddC and 3TC. Current data show that ddI is not able to re-sensitize AZT-resistant virus as originally thought. Though there is some return to AZT-sensitivity after using ddI, it is so short-lived as to be meaningless. When people switch back to AZT, AZT-resistant virus quickly recurs. Preliminary clinical data of AZT in combination with ddI indicate that while combination therapy may lead to greater suppression of viral replication, it does not delay the development of AZT resistance. Combination therapy may delay ddI resistance, however. Other studies are testing whether resistance can be delayed when ddI is used in combination with other drugs.

Resistance to d4T has not been studied extensively. Some of the test tube studies suggest that there may be some cross resistance between d4T and ddI/ddC and perhaps some cross resistance between d4T and AZT. Further research needs to be conducted on d4T resistance to understand how to use this drug most effectively.

For more information about HIV drug resistance, please visit or call the AIDS Survival Project Treatment Resource Center (404) 874-7926.

II. Other Antiviral/ Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs):

The non-nucleoside reverse transcriptase inhibitors (NNRTIs) were met with great enthusiasm when they were first discovered. These compounds (nevirapine; L-697, 661; TIBO; BHAPs) in test tubes were considerably more potent against HIV-1 than AZT and they had a better toxicity profile. However, when they were studied in humans there was rapid development of resistance (as quickly as within one week of starting therapy). This entire class of compounds was nearly dropped from further clinical development but interest was revived as a result of overstated claims made about a "three drug convergent therapy" approach. While the researchers later acknowledged flaws in the three drug convergent therapy report, they still believe the approach has merit compared to two-drug combinations and clinical trials studying this approach are underway.

Like the nucleoside analogs (AZT, ddI, ddC. d4T, 3TC), NNRTIs block HIV's infection of new cells. Reverse transcriptase is a part of HIV required to make new virus and infect more cells. NNRTIs stop the reverse transcriptase from working properly. The two types of NNRTI's you're likely to hear the most about are Nevirapine (Viramune) and Delavirdine.

Nevirapine (known as Viramune) [12]

Nevirapine blocks the reproduction of HIV in a different way than nucleoside analogues or protease inhibitors. By binding tightly to reverse transcriptase, nevirapine prevents viral RNA from being converted into DNA. In contrast, nucleoside analogues are incorporated into the viral DNA and make it ineffective. Protease inhibitors prevent copies of the virus from being successfully assembled and released from the infected CD4 cell.

Nevirapine has been approved for use in combination with nucleoside analog anti-HIV drugs in people who are failing their current treatment. Nevirapine is not approved for use with the protease inhibitor anti-HIV drugs (saquinavir, ritonavir, indinavir) as it is not yet known how these drugs may affect each other in the body. It is possible that taking nevirapine with protease inhibitors could be harmful to the liver.

What Does The Research Show?

The largest study of nevirapine was done in people with less than 350 CD4 cells. There were 398 people in the study. The average CD4 cell count was 138. Everyone had taken AZT, ddI or ddC for at least six months before starting the study. People were divided randomly into two groups. One group took AZT and ddI. The second group took AZT, ddI and nevirapine.

After four weeks, the amount of virus in the blood was reduced by about 90% in people taking AZT, ddI and nevirapine. However, after 48 weeks both groups had less CD4 cells than at the start of the study, but CD4 cell counts were around 30 cells higher in the AZT/ddI/nevirapine group. The amount of virus in the blood, or viral load, was slightly lower in the AZT/ddI/nevirapine group. In terms of disease progression or survival, 17% of people on AZT/ddI/nevirapine had a progression of disease or died, compared to 14% in the AZT/ddI group. This difference was not statistically significant, which means it could have been due to chance. This study did not show a significant benefit from adding nevirapine to AZT and ddI therapy.

Another study that has been presented divided 151 participants into three groups. No one in this study had taken anti-HIV drugs before. One group took nevirapine with AZT and

ddI. The second group took AZT with ddI. The third group took nevirapine with AZT. The average CD4 cell count was 376. After 52 weeks the 51 people in the nevirapine/AZT/ddI group had an average of 140 more CD4 cells than at the start of the study. The AZT/ddI group had 30 more CD4 cells than at the start of the study. The nevirapine/AZT group had the same number of CD4 cells as they had started with.

In this study, measurements of the amount of HIV in the blood are available after 28 weeks of the study. Both the AZT/ddI/nevirapine and AZT/ddI groups had a greater than 90% reduction in the amount of HIV in their blood after 28 weeks. It has been reported that about half the people in the triple combination group have viral loads lower than the test can detect. The nevirapine/AZT group had a large drop in the amount of HIV in their blood after four weeks, but were nearly back to where they had started after 28 weeks on the study.

This study shows that for people who have not taken anti-HIV drugs before, triple combinations of two nucleoside analog drugs and nevirapine can shut down HIV reproduction in the body very effectively.

What About Resistance?

HIV seems to get resistant to the effects of nevirapine very quickly unless the drug is used with two other nucleoside analogue drugs. If a person is resistant to nevirapine, they will likely be resistant to the other NNRTI that will soon be available, delavirdine. Information from two large clinical trials of delavirdine has been released, and is encouraging.

What About Side Effects?

The major side effect of nevirapine is a rash, which happened to 22% of people in studies. 6% of people in studies had a severe rash. 6.7% of people had to stop taking nevirapine because of this problem. This problem can be reduced by starting treatment at 200 mg. a day and escalating, or building up, to the higher dose of 400 mg. a day. If nevirapine causes a severe rash and you have to stop treatment, the company that makes the drug recommends that you DO NOT try the drug again. Other side effects can be elevated liver function tests, fever and muscle soreness.

How To Use It, Dosing and Drug Interactions

Start dose: Take one 200 mg. tablet once a day for the first 14 days. This lead-in period has been shown to reduce the frequency of rash. Inform your doctor if you experience any sort of rash or other side effect.

Maintenance dose; After the first 14 days, take one 200 mg. tablet twice a day thereafter, or as instructed by your doctor. Nevirapine tablets should be taken at 12-hour intervals, for example, at 7 AM and 7PM—whatever is most convenient for you. Do not increase your dose if you experience rash during the "starting dose" period, until the rash has cleared up.

Take Nevirapine every day as prescribed. Do not alter dose without consulting your doctor. If a dose is skipped, take the next dose as soon as possible; do not double the next dose.

You can take Nevirapine with or without food. Store Nevirapine tablets at room temperature (59 F to 86 F). Keep bottles tightly closed.

Nevirapine is processed in the body by the liver, like many other drugs. It has the potential to interact with commonly used drugs such as rifabutin, rifampin and ketoconazole and researchers advise that people be monitored closely for interactions if they are taking

other drugs with nevirapine. In studies, taking nevirapine with the antifungal drug fluconazole (Diflucan) increased the chance of getting a rash. For updated information on drug interactions, there is a medical information contact at the manufacturer that can be reached by calling (800)542-6257.

Nevirapine has no known clinically significant interactions with the following antiretroviral drugs: Zidovudine (ZDV), didanosine (ddI), or zalcitabine (ddC). However, Nevirapine may interact with other commonly used drugs. Be sure your doctor and pharmacist are aware of all the drugs you are currently taking. They can advise you about any possible interactions with Nevirapine.

Where to Get It

Nevirapine is an approved drug and is available by prescription through hospitals and pharmacies. Boerhinger Ingelheim/Roxane, the manufacturers of nevirapine, have set up a patient assistance program for people needing assistance accessing the drug. Call (800) 274-8651 for more information.

DELAVIRDINE (RESCRIPTOR)

Delavirdine (trade name Rescriptor) is another non-nucleoside reverse transcriptase inhibitors (NNRTIs).

What Does the Research Show?

Delavirdine has been shown in clinical trials to be well-absorbed by the body. Drug concentrations can be achieved in the blood that are 100 to 1,000 times the concentrations needed to inhibit HIV in the test tube. So far, the major side effect seen with delavirdine has been a rash, which develops in 20 percent to 25 percent of people taking the drug. This side effect can be reduced by starting treatment at lower doses of the drug and escalating to a full dose.

Clinical trials of delavirdine are ongoing. Early results from two trials have been presented. One study divided participants into four groups. One group took AZT alone. The second group took AZT and 600 mg. of delavirdine a day. The third group took AZT and 900 mg. of delavirdine a day. The fourth group took AZT and 1200 mg. of delavirdine a day. People in this study had an average T4 cell count of just over 300.

After 40-60 weeks, people in the higher dose (900 and 1200 mg. a day) delavirdine groups had T4 cell counts 35-70 cells higher than people taking AZT alone. People in these higher dose groups also had a 70% or greater drop in the amount of HIV in the blood, known as viral load, for at least 60 weeks. This study is ongoing, so how long this reduction in viral load will be sustained is not yet known.

The second study compared ddI taken alone to ddI and delavirdine at a dose of 1200 mg. a day. The average T4 cell count of people in this study was 135. There were no large increases in T4 cell counts in this study, although they remained above or near the baseline for at least a year. However, as in the previous study, a reduction in viral load of around 70% was sustained for at least 60 weeks.

Scientists also looked at information from these studies in another way. They matched the information about viral load to the actual health of the study participants. This was done to see if measuring the amount of virus in the blood can be used to monitor the health of a person with HIV. The results showed that viral load was very strongly linked to a persons health.

People who began the studies with a viral load of less than 10,000 had only a 1% chance of experiencing any disease progression during the 60 weeks for which information has been collected. People who started with a viral load of between 100,000 and 1,000,000 had a 6% chance of disease progression. People who started with a viral load of over 1,000,000 had a 24% chance of disease progression.

In addition, the effect of treatment in reducing viral load was also linked to improved health. This effect was most noticeable in people who started the studies with a viral load of over 100,000. For these people, a reduction in viral load of 70% or more, sustained for as little as 8 weeks, reduced their chance of experiencing any disease progression by 50% during the 60 weeks (over a year) for which information is available.

How To Use It, Dosing and Drug Interactions

Delavirdine can interact with other medications you may be taking. It is processed by a pathway in the liver that is used to process many other drugs, including the protease inhibitors. The following have been shown to reduce the levels of delavirdine in the body: rifabutin, rifampin, ddI and antacids. Several other drugs may interact with delavirdine; a list will be provided to those enrolling in the expanded access program. Also, it is recommended that delavirdine be taken on an empty stomach. The current dosage is 400 mg., three times a day.

Where To Get It

Delavirdine is now available through an expanded access program for people with less than 300 T4 cells. Your doctor can call (800) 779-0700 for more information, or you can call the Network for a description of the program and other delavirdine clinical trials.

III. Antivirals: Protease Inhibitors [13]

The interest in these drugs represents the largest investment yet in anti-HIV therapy by the pharmaceutical industry, a testament to their faith in the ultimate profitability of this approach. Although the production of practical and effective protease inhibitor compounds has proven difficult and expensive, several such drugs are now on the market and others are in clinical trials. Some have shown highly promising initial results.

How Do They Work?

Protease inhibitors act at a late stage of viral assembly, after the virus has been incorporated into a cell and is ready to begin mass production of new copies of the virus. Protease inhibitors have been shown to be effective in preventing the production of infectious virus in infected cells.

What Does the Research Show?

In general, protease inhibitors show very powerful anti-HIV activity in laboratory studies. However, they have proven very difficult to manufacture and while some have shown great promise in early clinical studies, others which looked good in the laboratory have failed. Still others are difficult to administer or are poorly absorbed when taken orally. Thus, there has been great variability seen so far in response to these drugs when they are given to people. Eventually, there is reason to believe that these technical problems will be solved and there should be several promising candidates.

Saquinavir (Hoffman-La Roche).

Saquinavir (also known as Ro 318959 and Invirase) was the first anti-HIV protease inhibitor to be studied in humans. Saquinavir is very potent against HIV in the lab, but the current formulation has poor bio-availability when taken orally. Absorption of saquinavir is only 4 to 6 percent, which means that people are getting very little of the drug into their bloodstream. Additionally, it is very difficult and expensive to manufacture. A new formulation of saquinavir is currently in studies in healthy volunteers to determine whether it has better bioavailability.

The phase I safety and pharmacokinetic studies show that the drug was very well tolerated with almost no side effects. The highest dose studied in the phase I trials was 600 mg. three times a day. At this dose there was some antiviral activity as measured by a drop in viral load and decreases in p24 antigen levels, accompanied by increases in CD4+ cell counts. However, the antiviral effect only lasted for about 16 weeks.

Initial phase II studies of saquinavir in people with 50 to 300 CD4+ cells who had at least 4 months prior AZT therapy showed that the drug seemed to work modestly well; the best results occurred in people treated with the three drug combination compared to the two drug combinations. Many researchers are concerned that most current studies may be using a less-than optimal dose of saquinavir.

A pilot study compares 600 mg. six times a day (3600 mg. a day) to 1200 mg. six times a day (7200 mg. a day) of saquinavir in people with 200-500 CD4+ counts. Preliminary data indicate that people who received the 3600 mg. a day dose had a greater reductions in viral load and greater increases in CD4+ counts compared to people who received the standard dose of 600 mg. three times a day. However, 35% of the participants receiving the 3600 mg. a day dose developed resistance after 20-24 weeks on therapy. No data are available on the 7200 mg. a day dose.

Two large phase III studies are now in progress to determine whether saquinavir is

able to delay disease progression.

Some preliminary resistance information is available from the European phase I studies. About 50% of the participants developed some degree of resistance to saquinavir after one year on drug. Although these data are preliminary, it may show some advantage in this regard for saquinavir compared to most other protease inhibitors, which have shown more rapid resistance.

Saquinavir is already approved and available by prescription. Hoffman-LaRouche has established a patient assistance program which can be reached at (800) 910-4687.

Indinavir (known as Crixivan, MK-639 and formerly L-735,524)

Merck's Indinavir is the second most-studied protease inhibitor. Initial results were very encouraging. There was a very significant reduction in viral load (99%), an often dramatic increase in CD4+ cell counts, weight gain, and p24 antigen levels went down to undetectable levels. However, virus levels began to increase again after 12 weeks and were back to original baseline levels at 6 months. Similarly, CD4+ cell counts were also returning to their baseline levels. Even this result, how ever, does not paint a picture worse than existing therapies, and in some ways is better. The most interesting aspect of the study of Merck Indinavir is that highly positive results, though short-lived, were seen in advanced stage patients, people who entered the study with very low CD4+ cell levels and who had previously used and failed on other existing antiviral drugs. This finding gave new hope to the thought that the immune system might restore itself, even in late-stage disease, if a high enough level of virus suppression could be obtained. The most recent data from studies of this drug in healthier people seem to show that the improvement in CD4+ levels may extend well after virus levels have begun to increase again. Most study volunteers still had elevated CD4+ counts a full year after the start of the study. T his raises many important questions which will only be answered by the longer-term studies currently underway.

Other studies of this protease inhibitor include combinations with AZT and with AZT plus ddI. Initial reports indicate few side effects. A few study volunteers experienced increased liver enzyme levels, and there are early reports that people receiving the highest dose levels (1000 mg. 3 times per day) sometimes experienced kidney stones. Further studies will focus on a dose of 800 mg. 3 times daily, where these effects have not been seen.

Resistance to Indinavir has also been seen in clinical studies. The phase I studies show that some degree of resistance occurs after 12- 16 weeks on Indinavir with a corresponding decrease in CD4+ cells and an increase in viral load. Data on a small group of volunteers who continued to take Indinavir at the end of the phase I study show that not only do they develop some resistance, but they also show some cross resistance with all of the current protease inhibitors now in development. Manufacturers of some of the other drugs, however, question this finding. Merck is now exploring higher doses of this drug as well as combining it with AZT, AZT and ddI, AZT and 3TC and d4T to determine whether these strategies may delay resistance to both Indinavir and the nucleoside analogs.

Merck is approved and available by prescription, but currently only through Stadtlanders Pharmacy (1-800-927-8888).

Ritonavir (Norvir - ABT-538 - Abbott Laboratories)

Abbott Laboratories also has an approved protease inhibitor called Ritonavir (also known as ABT-538, formerly A 84538). Preliminary data are very encouraging. A phase I/II study conducted in Europe enrolled 80 men with greater than 50 CD4+ cells and who were p24 antigen positive. Participants were given one of four doses of the drug twice daily or placebo. Participants who received the two lower dose levels experienced a sharp drop in viral load and an increase in CD4+ cell counts, however after 12-16 weeks viral load and CD4+ cell counts were both returning to their original levels suggesting the onset of resistance. Participants who received the higher dose levels also had a sharp drop in viral load (to undetectable levels) and a big increase in CD4+ cells (averaging between 300 and 400 cells) which was sustained for 12 weeks. These people are still being followed. T he only significant side effect noted was a temporary increase in liver function tests. Results from a US study of ABT-538 showed similarly promising results. Resistance to Ritonavir from the human clinical studies has not been widely reported although based on test tube studies, resistance has been clearly demonstrated. There have been reported problems with the stability of this compound with a reported shelf life of two weeks. Nonetheless, Ritonavir appears to be a highly active and very promising compound. Ritonavir has been approved and is available with a prescription.

Nelfinavir(known as Viracept and AG-1343) [14]

Nelfinavir (Viracept), a new protease inhibitor from Agouron, has been shown to be a very active and well tolerated agent for treating HIV, when use alone, in dual combination with a nucleoside analogue, and, especially, in triple combination therapy.

Monotherapy. In a phase-2 dose ranging study, monotherapy with nelfinavir at 500, 750, or 1,000 mg. doses three times a day demonstrated that the drug was safe and highly active at all three doses when randomly assigned to 30 HIV-positive patients for 28 days, reported Dr. Marcus Conant, of the Conant Medical Group in San Francisco.

Upon completion of the study, patients were given the opportunity either to continue monotherapy or to add reverse transcriptase inhibitors. The individuals who continued on monotherapy for an additional three months continued to derive benefit, but those who added either AZT and 3TC or d4T to their nelfinavir for a further five months showed significantly greater reductions in viral loads, as well as larger increases in CD4 cell counts than those on monotherapy.

Double combination therapy. Data from the most recent study confirm nelfinavir's activity and safety when used in combination therapy, with nelfinavir plus d4T being two-to-threefold more effective than d4T alone, stated Dr. Joseph Gathe of the Montrose Clinic — Houston Clinical Research.

In a 60-day, phase-2 study, 39 HIV positive patients with CD4 cell counts of 200 and HIV RNA counts greater than 15,000, none of whom had ever received a protease inhibitor or d4T, were randomized to one of four treatment groups: d4T 40 mg. twice daily plus either 500, 750, or 1,000 mg. of nelfinavir three times daily or d4T alone. Ten patients dropped out of the study, chiefly because they wanted other drug regimens.

Overall, patients in the nelfinavir treatment groups who continued the two-drug therapy through five months reported mean viral load reductions of 1.3-1.9 log and CD4 cell increases of 87-111. Persons who had been on d4T monotherapy also received increased therapeutic benefit after adding nelfinavir to their regimen following the initial 60-day study.

Triple combination therapy. Combination therapy with nelfinavir, AZT, and 3TC in antiretroviral-naive patients resulted in undetectable levels of HIV RNA in plasma as well as peripheral blood mononuclear cell (PBMC) co-cultures, suggesting great promise for controlling HIV replication in these individuals, according to Dr. Martin Markowitz of the Aaron Diamond AIDS Research Center and Rockefeller University in New York City.

Twelve antiretroviral-naive patients with baseline viral loads of 18,000-865,000 were treated with nelfinavir 750 mg. three times daily, AZT 200 mg. three times daily, and 3TC 150 mg. twice daily. Baseline median CD4 cell count was 253. By 12 weeks of therapy, HIV viral load was undetectable (fewer than 500 copies/ml) in 11 eligible patients, with a mean drop of 2.62 logs. At week 16, all patients were aviremic— that is, no virus could be detected in plasma. At week 20, there were no new HIV-related infections or neoplasms, and either resolution or marked improvement was seen in a variety of HIV-related conditions. The trial is ongoing to determine the durability of viral suppression with this triple-drug regimen and to attempt to determine the significance of prolonged aviremia.

Expanded Access Program: On September 16, 1996, Agouron Pharmaceuticals, Inc. announced the availability of Viracept through an expanded access program. The program is for people with advanced HIV disease who have exhausted all current protease inhibitor treatment options. People who are unable to take any of the three approved protease inhibitors due to intolerance and have a CD4 count of 50 or less qualify for this program. The number to call for Viracept expanded Access program is (800) 621-7111.

KNI-272 (Kyoto/National Cancer Institute) [15]

Kyoto Pharmaceutical University is jointly developing their protease inhibitor KNI-272 with the National Cancer Institute. KNI-272 is currently in phase I studies at the National Cancer Institute. Preliminary data show that it has similar resistance patterns to the Merck compound. Work is underway to develop analogs to KNI-272 so that resistance patterns will be different from the other protease inhibitors.

Other Protease Inhibitors

There are numerous other companies that are developing protease inhibitors with several likely to be in human clinical studies during 1996. These include Vertex/Glaxo-Wellcome, Pfizer, DuPont , Merck, Parke Davis, Lilly, Searle, SmithKline Beecham, Ciba-Geigy, Hoechst/Bayer, Lucky Pharmaceuticals, Boehringer Ingelheim (BioMega), Sandoz, and Takeda Pharmaceuticals.

Access and Use of Protease Inhibitors

Availability of Protease Inhibitors

Only Saquinavir and Ritonavir have been approved by the FDA in the US or by any regulatory agency in any other country. Merck expects accelerated approval in spring of 1996. Access to most protease inhibitors is generally available only through clinical studies, however most of these studies are randomized controlled trials which means a volunteer risks the possibility of being randomized to the control group (usually a nucleoside analog). At the end of these studies, most sponsors will make the protease inhibitor available if it proves to be superior to the control drug. Expanded access/parallel track programs ended recently when enrollment was filled and a waiting list developed. The AIDS Survival Project Treatment Resource Center keeps updated information on dug studies and availability, (404) 874-7926.

Resistance to Protease Inhibitors.

Test tube studies show that resistance can develop to all known protease inhibitors. Most of the clinical studies of protease inhibitors used as monotherapy indicate that some degree of resistance develops after 12 weeks of therapy. As with the nucleoside analogs, resistance is likely to develop at different rates at different stages of disease progression. There is some cross resistance between the different protease inhibitors. Current test tube studies show that resistance patterns for the protease inhibitors fall into two separate categories, although clinical studies seem to indicate that many random patterns are involved. Several clinical studies are now ongoing or planned to determine if resistance can be delayed by combining multiple protease inhibitors or by combining one or more with reverse transcriptase inhibitors. If such combinations slow the development of resistance to either or both types of drug, it will likely extend the clinical benefits of therapy. It is also important to be compliant in taking these drugs as skipping a dose or taking too low a dose may also lead to more rapid development of resistance.

Participating in Protease Inhibitor Studies.

It is important to consider, before participating in a study with a protease inhibitor, that you may be disqualified from future studies involving other antivirals. The reason for this is that because of exposure to another protease inhibitor, this person may not receive the expected full benefits of a new drug in terms of antiviral effects, with the second protease inhibitor. Pharmaceutical companies want to be able to get the "best and cleanest data" available and therefore exclude people who have been on a similar drug. T his practice may be both unfair and impractical.

With the possible exception of the Upjohn drug, most of the current generation of protease inhibitors are unlikely to be able to cross the blood-brain barrier due to the large size of the drug molecule. Since the brain is a potential reservoir for HIV, combining protease inhibitors with another drug that crosses the blood brain barrier (like AZT) seems a likely strategy.

Protease Inhibitors - The New Era in AIDS Treatment: One Chance to Use It Right or Lose It [16]

Recent announcements of interim results from studies of the new protease inhibitors ritonavir (Abbott) and indinavir (Merck) signal the most potent assault yet on HIV. One study of ritonavir showed a 50% reduction in the death rate over five months in people with advanced disease. A small study of indinavir showed that when it was used as part of a three-drug combination with AZT and 3TC, 90% of the people saw their virus levels drop below detectability. All is not perfect in this era, however. A careful look at the data thus far, along with accumulating knowledge of how protease resistance (and multi-drug cross-resistance) develops, leads to a sobering conclusion. *However potent these drugs may be, they must be used with great care and deliberation. Without carefully chosen strategies, their benefits will be short-lived and quickly followed by the development of multi-drug cross-resistance to most of the field of protease inhibitors.* This multi-drug resistant virus could be transmitted to others. This situation closely resembles that of tuberculosis, where improper use of therapies will actually make things worse by inducing development of multi-drug resistant stains of the organism.

Unlike nucleoside analogues like AZT or ddI, resistance to one protease inhibitor often confers resistance to many others. For example, when a person becomes resistant to Abbott's ritonavir, Merck's drug will also become relatively impotent. The same cross-resistance is then likely to apply to Agouron's nelfinavir. The only slight escape comes for people who might first develop resistance to Roche's saquinavir; its resistance confers only one of four mutation steps needed to develop cross-resistance to the other protease drugs. Still, even this first step sets the necessary conditions for, and hastens, the eventual development of multi-drug resistance. Similarly, resistance to ritonavir or indinavir may not automatically confer later resistance to saquinavir, but does take some initial steps in that direction.

The risks of failing to address resistance are readily seen in the Abbott "salvage" study which tested ritonavir in people with advanced disease (CD4+ counts under 100). Everyone applauds the idea of testing new drugs in this group, but the protocol design created as many problems as it solved. The study randomized volunteers to receive either ritonavir or a placebo, which was added to whatever other therapy the person happened to use (or to no other therapy). There was no strategy for dealing with the resistance question. Some saw this as a welcome step toward a "real world" model of drug testing, arguing that this is just how people are likely to use the new drug. Others, however, viewed it as a sanctioned way of using a new drug improperly or at least not optimally. Lack of optimal use might not be much of a problem if the only impact were on the reputation of the drug, but in this case, it had clear health implications for the patient volunteers.

Five months into the trial, both supporters and critics saw what they wanted. On the positive side, the group receiving the drug had about a 50% reduction in the death rate and a similar reduction in new AIDS-defining infections compared to those who received a placebo. But this was only part of the story. Less discussed was the fact that people receiving the drug saw only an average 1.6 log drop in their viral load early in the study. (For more information about understanding logs, call Project Inform at 1-800-822-7422.) After five months, their viral load was rising quickly, showing only a .6 log reduction, signaling the onset of viral resistance. The size and duration of the viral load drops were lower than

those in some other protease studies. Very likely, the study volunteers were quickly becoming resistant to ritonavir. With longer follow-up, the clinical and survival benefits would likely have been shown to diminish. While people saw a short term reduction in death and new infections, the sub-optimal "real world" protocol design also reduced the overall potential impact of the protease inhibitor (compared to that seen in more structured studies). Used in this fashion, the initial benefits from a protease inhibitor may be over in six months, with little or no prospect for future benefit from this class of drugs. Some argue that if that's the "real world" outcome, then so be it since that's the way people will use these drugs. They maintain that at least there was some benefit, and that this trial tells us what we can realistically expect from a single protease inhibitor used in this fashion, in this population. Such reasoning seems based on very low expectations, both about the drugs and peoples' ability to act rationally.

Others studies suggest that far more potent and lasting results are possible if the new drugs are used strategically in combinations. In earlier studies of indinavir monotherapy, sub-optimal use diminished its potency and hastened resistance. More recent studies have sought to optimize its impact by using it in combination with a second and third drug. Used in three-drug combinations, both the size and duration of antiviral effect were greatly enhanced compared to the "do whatever you want" trial of ritonavir. People receiving two different three-drug combinations including indinavir fared far better than those using single agents or two-drug combinations. The same studies showed that the choice of the other drugs used in the combinations also matter. But in all the indinavir three-drug combinations, extent and duration of antiviral effect were enhanced and drug resistance was not in evidence at six months. Other studies of ritonavir are also looking at specific combinations and there is reason to expect excellent results from these.

Studies of high-dose saquinavir at Stanford University add yet another wrinkle to the story. New data from these studies indicate that if people are careless or sloppy in their use of these drugs; for example, by skipping doses occasionally or reducing dosage, the almost certain outcome is far more rapid development of resistance.

The clear conclusion is that *how* these drugs are used will impact enormously on how well and long they work. Furthermore, no other entirely new class of drugs is remotely close in the pipeline so it is not realistic to expect, as in the days of nucleoside drugs, that "something else" will soon become available when the protease drugs fail.

In short, people and their physicians must learn to use these drugs correctly, or they will quickly be rendered useless as a class of agents. The comparison to tuberculosis is obvious. Effective treatment of that disease requires a carefully chosen combination of drugs, employed with almost religious fervor, for the duration of treatment. Inadequate combinations, low doses, or sloppy, undisciplined use hastens the development of multi-drug resistant strains of tuberculosis. These strains become largely untreatable in the patient, and they can be passed on to others in all the ways TB is normally transmitted. Health officials and scientists wouldn't dream of sanctioning sub-optimal use of TB therapies by shrugging and declaring it the "real world." Instead, they have created aggressive education campaigns teaching patients and physicians alike about the critical importance of using these therapies properly. Nothing less is called for in AIDS. In this regard, it is critical that the FDA makes sure that labeling and standard-of-care recommendations address this issue.

Making Decisions: Optimal Use of Protease Inhibitors

While final answers on the best use of protease inhibitors will require years of study, some hints can be seen for people who cannot, or will not, wait. To start, there are a few things which help distinguish "worst case" from "best case" use.

WORST CASE SCENARIOS:

These scenarios are least desirable and most likely to lead to rapid multi-drug resistance

- ***Using a protease inhibitor alone,*** especially in advanced disease. The only time it would be reasonable to use a protease inhibitor alone is when a person simply cannot tolerate or access other drugs for use in combination.
- ***Using an inadequate dose.*** If adequate dosing is impractical, as with the early formulation of saquinavir, this can be minimized by using the best other available agents along with it in a three-drug combination.
- ***Reducing the dose below the prescribed level,*** even if temporarily. If intolerance or side effects develop, it will be better to temporarily stop the drug rather than reduce its dose. This runs counter to common clinical practice with the older nucleoside drugs, in which physicians routinely lowered dose as a way of dealing with side effects. The fastest way to develop resistance is to use the protease inhibitor at an inadequate or inconsistent dose level.

SUB-OPTIMUM USE :

These scenarios induce some risk of diminished effectiveness and more rapid resistance

- ***Adding a protease inhibitor on top of whatever else a person is doing,*** without consideration of drug resistance.
- ***Adding a protease inhibitor to only one other drug.***
- ***Adding a protease inhibitor*** to another drug or a two-drug combination ***without careful selection*** or knowing the current effectiveness of the other drugs used.

BEST CASE SCENARIOS:

- ***Beginning a protease inhibitor at about the same time as two other new drugs*** for combination use or at least with two drugs which haven't been used for a long time. If all or most other drugs have been used previously, it would be important to use the protease inhibitors with a combination which has proven synergy, such as AZT plus 3TC.
- ***Using a protease inhibitor with the most potent two or three other drugs,*** all of them for the first time (prior to any opportunity for resistance). This, however, leads to the unanswered question, "When to Start?"
- ***"Pretesting for drug sensitivity"*** before beginning a new combination (a technology not commonly available, to test drugs against the virus to insure they have activity prior to initiating therapy).

Difficult Questions/ Few Answers

A critical question, still unanswered, is when to begin using a protease inhibitor at all. Underneath this lies the issue of when to begin therapy of any kind. The answer might be fairly obvious in some situations, less clear in others. Most researchers agree that use of a protease inhibitor would be clearly indicated when:

- a person has shown evidence of disease progression;
- there is evidence that existing therapies aren't working, as measured by viral load, CD4+ cell decline, or clinical condition and events;
- a person has a "high" viral load, regardless of clinical condition or CD4+ counts (one new study reports that even viral loads above 10,000 predict a higher risk of progression, so the definition of "high" may need to be revised).

Increasingly, researchers are also interested in testing three-, or four-, drug combinations (including protease inhibitors), or administering protease inhibitors in people who have recently been exposed to HIV, such as health care workers stuck by an infected syringe. A similar idea of "hit it hard and hit it early" is being suggested for people known to be in or just beyond the "acute infection" stage—a period of flu-like illness which often occurs a month or so after initial infection with HIV. The hope of aggressive treatment is to either stop the infection altogether, or at least minimize its potential for long-term damage by lowering viral load.

Lack of data makes it unclear if a similar "hit hard and hit early" philosophy is always right for everyone:

- Should all HIV-infected people, regardless of CD4+ cell levels or viral load, be treated immediately with the most potent multi-drug combinations? Some scientists believe this is appropriate, at least as a research question. Others fear even the best therapies will not work indefinitely and using them in relatively healthy people or people with low viral loads might waste our best weapons in many people before they are needed.
- In some people, will therapy with drugs like the AZT/3TC combination be sufficient to sustain low viral load? In this case, does adding a protease inhibitor help in any way?
- Do people with low viral levels, say under 5,000 on the PCR test, require therapy at all? If viral load drives disease progression, why use therapy when viral load is already low? Does using the drug simply create the opportunity to develop viral resistance, without adding to clinical health? Or, at the other extreme, might using a protease combination early on make it possible to suppress the disease for very long periods or even permanently?
- In general, should the decision to initiate therapy be based on viral load instead of CD4+ counts, as some recent studies suggest, or should both be taken into account?

These are difficult questions. There are many opinions but very little hard data. There are data, however, that indicate that at least a small subset of HIV-infected people fare very well for long periods without therapy. Some researchers argue science must not upset this balance in such people. But, it may be equally valid to test therapy in such people to see whether, with a little more help, the body might be able to rid itself permanently of any risk of symptomatic disease. But for now, both views are equally valid and in need of research.

One thing is certain: *how* these drugs are used will be critical. Test centers are already seeing newly diagnosed patients with AZT-resistant virus. If protease drugs are misused, it won't be long before we see newly infected people who begin their HIV-infection with multi-drug, cross-resistant virus. A new wave of clinical trials must be initiated immediately to address treatment strategy. A massive educational campaign must begin to teach physicians and patients all that is known about the proper use of these drugs. Approval of these drugs should not be structured in a way that permits pharmaceutical companies to say their work

is finished and wash their hands of further research. Nor can we permit the federal apparatus, led by the Office of AIDS Research, to turn away in pursuit of easier, less complex work in the field of basic science, and shy away from the difficult task which lies ahead.

Similarly, the advent of protease inhibitors and their impact on viral load make it more necessary than ever that viral load testing be a routine part of the standard of care for HIV-infected people. It is time for the debates to end and for the third-party payers to stop whining about costs. The expense of mismanaging the treatment of AIDS is the real cost with which they should be concerned. Viral load testing will tell physicians when it is time to start therapy, time to change therapy, and time to withhold it. HIV medicine cannot be intelligently practiced without this critical tool.

Protease inhibitors may meet their potential as the largest leap yet in AIDS treatment, or they may become only a footnote on the way to an era of a new form of multi-drug resistant HIV infection. The difference is up to us.

LEADING HIV-1 PROTEASE INHIBITORS

MANUFACTURER	Roche	Merck	Abbott	Agouron	Glaxo Wellcome Vertex
TRADE NAME	Invirase™	Crixivan™	Norvir™	Viracept™	TBD
GENERIC NAME	Saquinavir	Indinavir	Ritonavir	Nelfinavir	TBD
COMPOUND NAME	Ro 31-8959	MK-639	ABT-538	AG1341	141W94 (VX-478)
FDA APPROVED	Yes	Yes	Yes	Phase II/III Clinical Trials	Phase I/II Clinical Trials

Protease Inhibitors At A Glance [17]

	Crixivan (Indinavir/Merck)	Norvir (Ritonavir/Abbott)	Invirase (Saquinavir/Roche)
What is the correct dose?	Four 200mg (or two 400mg) capsules every 8 hours on an empty stomach. (You can take it with a piece of dry toast and black coffee; but **no** fat at all.)	Six 100 mg capsules every 12 hours with food. Talk to your doctor about starting at a lower dose to avoid side effects. ***NOTE: This medicine contains alcohol.***	Roach says to take three 200mg capsules 3 times a day (1800 mg), but some doctors suggest 3600 mg or even 7200 mg a day (3-18 pills a day)
How should I store it?	Keep in cool, dry place.	Keep in your fridge.	Keep at room temperature.
What is the effect on disease progression?	Unknown. There is clinical trial in progress to determine effect on disease progression. The only data so far is on viral load and T-cells, not on preventing illness.	In a big trail, people with less than 100 T-cells took Norvir and whatever combination of antivirals they wanted. People who took Norvir had half as many OIs and half as many people died. There is no information on people who have less advanced HIV infection.	Unknown. There is currently one trial open studying a new formulation of Invirase in 600 people with less than 500 T-cells.
What is the effect on the virus?	The amount of HIV in blood can be reduced by 100 times (e.g., by 100,000 to 1,000 copies). This has been seen in the lymph nodes too, in a few people studied. We are told that about 20% of the drug is absorbed into the brain.	The amount of HIV in blood is reduced by up to 100 times on average. No information on how it works in lymph nodes, and only 1% of Norvir gets into your brain.	The amount of HIV in the blood is reduced by up to 55% when drug is taken with AZT or ddc. It is not known how combinations affect viral load in the blood, lymph, or brain. ***The drug is only for use in combinations.***
How long does the antiviral effect last?	In small numbers of patients, the effect on the virus lasts six months to one year in 40%-60% of people who take Crixivan alone. Although the effect seams steady, we don't know how long or how strongly the effects last.	Unknown. No information on people who have taken Norvir for longer than four months. In advanced patients, the antiviral effect seems to decrease between the second and fourth month of therapy.	In Invirase is taken alone, the effect is less than AZT taken alone and lasts for about six months longer. It lasts longer if Invirase is taken in a combination.
What is the effect on CD4 counts (T-cells)?	On average, CD4 counts increased by about 100 and seem to stay up for six months to a year in most of the few patients who have taken the drug for that long.	In most studies, CD4 counts increase between 30 and 60 T-cells, but the follow up is very short.	On an average, CD4 counts increase 40 to 70 T-cells within the first few weeks of treatment but taper off between four to six months, even in combination.
Can it be used with other anti-HIV drugs?	Yes. Combinations with AZT & 3TC and AZT & ddI were well tolerated. In fact, early data suggests that combination therapy may delay resistance. ***NOTE: It is recommended that ddI and Crixivan be taken at different times of the day and both on an empty stomach.*** **HELLO!!! When do we eat?????**	Poorly tolerated. Two out of five people who took Norvir and AZT dropped out of the study. One of three who took Norvir, AZT and ddC dropped out. In fact, because it is so hard on your stomach, it is recommended that you start with two weeks of Norvir alone and/or start at a lower dose to get use to it. It is supposed to get better.	Yes. Some felt nauseous, weak, and had stomach pain when they took Invirase and AZT or ddC, but the combination of ddC and Saquinavir extends people's lives compared to monotherapy. Resistance is delayed with combination antiviral therapy. There is a clinical combining Invirase and Norvir, but we have **NO** idea if this is safe at all.

Protease Inhibitors At A Glance

	Crixivan (Indinavir/Merck)	Norvir (Ritonavir/Abbott)	Invirase (Saquinavir/Roche)
Can it be used with other types of drugs?	**Do not take**: rifampin, Hismanal or Seldane, Halcion, Propulsid, Versed, antacids. **Change dose**: Nizoral, Mycobutin and rifampin. All these medicines get processed by the liver and the amount of Crixivan you absorb will change if you take these as usually prescribed. **Check with your pharmacist before taking anything, even over the counter, with a protease inhibitor.**	**Do not take**: Luminal or Solfoton, Tegretol, Invirase, antacids, dexamethasone, Flagyl, Dilantin, rifampin, tinidazxole, Mycobutin. **Change dose**: Biaxin, Norpramin, Antabuse, ketaconozole, contraceptives, and broncodilators. Tell your doctors you are taking Norvir if they prescribe any drug to you. The list provided by Abbott is not complete. Hey! Anything can happen!!!!	**Do not take**: rifampin, Mycobutin Luminal or Solfoton, Dilantin, dexamethasone, Tegretol, Hismanal and Seldane. Check with your doctors for antacids, heart medicines, asthma medicines, antifungals, sedatives,. pain killers, antibiotics, and Dapsone. Invirase is poorly absorbed by your body and a lot of drugs make the absorption even worse, so check it out with your doctor!
What are the side effects?	Crixivan causes low back pain due to kidney stones in 2%-3% of patients. You can reduce your chances of this by drinking lots of extra water (like 8-10 glasses a day). Bilirubin levels go up in the blood, but this does not seem to cause any problems.	Lots of side effects: nausea, vomiting, tingly lips, gas and diarrhea, which have forced people to stop taking the drub. Up to 25% of patients using Norvir alone stopped, and 38% of people stopped who took it in combination. We have no data on the new formulation that they claim is gentler--but some people report it is not different. Norvir makes triglyceride levels (a type of fat) go up, but we do not know if this is necessarily causes any problems.	Of course, a few people have strange (and dangerous) reactions to Invirase, but overall, it is easier on your system than AZT. Most of the side effects have to due with the fact that you have to take so much Invirase to have any get into your system. Roche is studying a new formulation that may be easier to absorb. This should reduce stomach side effects.
How important is it to take the drug exactly as prescribed?	**VERY IMPORTANT! Missing doses or taking lower doses might result in your virus becoming resistant to Crixivan and all other protease inhibitors** (*cross resistance*). The drug, however, was well tolerated in clinical trials. More than 90% of patients took this drug, even in combination, without stopping.	**VERY IMPORTANT! Missing doses or taking lower doses might result in your virus becoming resistant to Norvir and all other protease inhibitors** (*cross resistance*). The drug was not well tolerated in clinical trials. 25% of patients stopped taking the drug when used alone and more than one out of three people stopped Norvir in combination trails. **This is a very important consideration if you decide to take Norvir because of the potential for cross resistance.**	**VERY IMPORTANT! Missing doses or taking lower doses increases the chances of HIV becoming resistant to Invirase**. It seems that most resistance caused by Invirase is different than resistance cause by Crixivan and Norvir. If Invirase stops working for you, the other protease inhibitors will still be an option, most likely.
Where is the drug available?	*Only* through Stadtlanders, a mail order pharmacy: 1-800-927-8888. Merck's patient assistance program: 1-800-850-3430.	In most pharmacies today. Patient assistance: 1-800-293-4393.	Drugstores all over the U.S. Patient assistance: 1-800-282-7780.
How much does this drug cost?	Less than a ton. Merck sells Crixivan for $4,380 a year, yet Stadtlanders charges individuals $6,022, a 37% markup!!! Insurance companies get it for less!!!	A ton, or about $8,000 per year.	A veritable bargain at $7,600 a year.

Protease Uninhibited

Some things to keep in mind about Protease Inhibitors.

1. *Not all protease drugs are alike.* Their effectiveness, the kinds of resistance they cause, side effects, how well they work in combination with other drugs, and what kinds of antibiotics, antivirals, antihistamines and birth control you can use at the same time are different with each drug.

2. *Two of these drugs,* Crixivan and Ritonavir, *are the strongest anti HIV drugs to date.*

3. *Taking protease drugs with other antivirals*, like AZT/3TC, ddI, d4T, etc., may make them stronger and help the effect last much longer than just taking one protease alone.

4. *There is a lot of variation in how people respond to these drugs*. In trials, some people have had fantastic T-cell increases and viral load drops. Other people had very little response.

5. *Taking a protease drug requires a different kind of commitment from you than any previous anti-HIV drug.* Be clear with yourself before starting that you can really commit to the drug as prescribed, each and every time period. WHY? Because antivirals can only work if HIV is not resistant to them. Avoiding resistance for as long as possible is the key to getting the most of the protease drugs. If you skip doses, even a few times, or less than prescribed, your HIV may become resistant. IN early protease trials, people who took lower doses developed many different kinds of HIV resistance, and now none of the protease drugs will work for them.

6. *Taking one can make you resistant to the others.* Saquinavir can cause a partial resistance, but in some cases, full cross resistance. Taking Crixivan or Ritonavir will make you resistant to all other protease inhibitors. This is called cross resistance. It means you can probably only benefit from one of the powerful protease drugs. Once your HIV gets resistant to one you choose, no other protease drugs will work for you.

So, it's worth taking the time to figure out your protease strategy.

Check which drugs you take with each on them, how often you take them, and what side effects you might expect (see chart on pages 4-5). Consider getting a viral load test to measure what HIV is up to in your blood. Choose which drug(s) you want to try, if or what other antivirals you want to take at the same time, and consider whether you can really commit to following your strategy 100%.

How can you tell if your HIV is becoming resistant to a protease drug (or 3TC/AZT or ddI, etc.)?

By taking a viral load test. If your numbers are high, say 300,000, and you start a drug, your numbers should fall in a month. If they stay the same or go up, then the drugs are not working very well for you. It is more confusing if your viral load is low. Is it the drug, your immune system, or both that are keeping your virus low? You may talk to your doctors--keep watching your viral load. In time, we hope to better understand how to use the viral load test.

Some big unresolved questions.

√ What is the best drug combination to keep HIV and resistance low?

√ What are the long-term safety issues?

√ Lots of people agree that PWAs with high viral loads and symptoms, who have taken AZT and other drugs for years, might want to try protease. What about everyone else?

√ What is your viral load is high, but you have no symptoms? Many argue that keeping HIV as low as possible is the key to survival. Others worry about getting strong resistance before having any symptoms.

√ What if viral load is very low--under 10,000? Taking combination antivirals may keep it low, or maybe your immune system would do that anyway. Maybe a strong protease combination will kick you into some kind of remission, with no progression for years. Or maybe it will not change much, except to cause your HIV to become so resistant that you cannot get any benefit from antivirals if your T-cells fall later.

WE HAVE NO IDEA.!

What is the best way to use Protease Inhibitors?

To make sure your body gets the full benefit from protease inhibitors, you must be aware of the things you can do to help your body better absorb these drugs.

√ Take Invirase (Saquinavir) within two hours of a full meal or a substantial snack.

√ Take Norvir (Ritonavir) with a full meal that is high in fat and protein.

√ Take Crixivan (Indinavir) on an empty stomach, one hour before or two hours after meals, with a large glass of water. Drink at least 48 ounces of liquids daily to maintain hydration. You can take your Crixivan with a light meal, low in fat, if you need to. A light meal might be plain toast with juice or skim milk.

What can you do to prevent the development or resistance?

√ Take protease inhibitors in combination with one or two other kinds of anti-HIV drugs. Do not do combination therapy with two protease inhibitors; we still do not have enough information to support the use of two protease inhibitors at the same time. Figure it out with your doctor or by yourself, with the help of treatment advocates, which combination works better for you

√ Take full dose prescribed by your doctor everyday..

√ **If the side effects are intolerable** do not reduce the does. Do not skip a dose. And do not take it every other day. The best thing to do is to stop the drug altogether. Talk to your doctor about starting again.

√ **Do not take "drug holidays."** You must not skip a dose. If you want the full benefit, you have to be good and keep taking the drug everyday. Remember once you have resistance to one of the protease inhibitors, you may not benefit from the others.

√ **If you miss a dose by more than 3-4 hours, wait until the next scheduled dose.** Do not double the next dose. But if you miss a dose by less than two hours, go ahead and take the next dose at the regular time.

There's more to life than AZT alone
An Introduction to Protease Inhibitors

What is a Protease Inhibitor?

Protease (pro-tee-ace) inhibitors are a new group of drugs. They fight HIV directly. Some are approved and some are still experimental. Believe it or not, there are about 20 different kinds of protease inhibitors. They have different strengths. Some are close to approval. Others are just getting studied.

How do you do the things you do?

In order for HIV to cause damage, it needs to reproduce over and over. This takes many steps. The enzyme *protease* is one important step. HIV needs this enzyme so it can make copies of itself. These drugs stop the protease enzyme.

Are these drugs like AZT?

NO. AZT, ddI, ddC, d4T, and 3TC are a different family of drugs. They are called *nucleoside analogues*. They work against HIV by trying to stop a different enzyme--one called *reverse transcriptase*. AZT-like drugs work well in some people, but not in everyone.

Why not? First, these drugs are no specific. They may attack lots of white blood cells, even ones that do not have HIV in them. Second, these drugs can cause serious side effect. Third, they stop working in most people in 6-12 months.

What else? AZT-like drugs are not as strong against HIV as some of the protease drugs. Also, they only protect white blood cells that are not infected. They do not fight the HIV that's already in the cell. Protease inhibitors can enter infected cells and stop HIV from reproducing.

So far, protease inhibitors seem much safer than AZT and the other nucleoside analogues. They are so specific that they do not hurt your bone marrow or other white blood cells, but there is *no* date on long-term safety.

Are there any problems with protease inhibitors?

Yes. With all drugs that fight HIV, like AZT or 3TC or protease inhibitors, *resistance* can be a big problem. *Resistance* happens when HIV learns to keep growing in spite of a drug. When HIV is *resistant* to a drug, than drug can no longer fight HIV.

If your HIV learns to get around AZT, you can (if you want) switch to ddI. This is probably **not** true with protease inhibitors. Taking one protease drug might change the HIV in your body so that no other protease will work for you. This is called *cross resistance*. **Unfortunately, it seems that all the protease inhibitors can cause cross resistance, although it might *not* happen on an individual basis**.

Can resistance be stopped?

The HIV virus is very smart and can learn to resist a lot of drugs. However, we hope that combining drugs (taking more than one anti-HIV drug at a time) will confuse HIV. When drugs are combined, HIV has a harder time learning to get around the drugs. And if a combination does not stop resistance, it might slow it down.

Some doctors feel that protease drugs should be taken with other anti-HIV drugs like AZT and 3TC to slow down resistance. We have no idea right now if this will work. Hopefully, trials studying this combination will let us know.

Are there any side effects from taking protease inhibitors?

Like so many things that appear to help us fight HIV, there are side effects with protease inhibitors.

First, you will have to take a lot of these drugs for them to work. The body cannot absorb protease very well. Taking a high amount of any drug can often mean trouble for your liver, kidneys, and stomach. They more drug you have to take, the harder your liver needs to work to break it down, causing problems.

Second, there are many drugs you will not be able to use depending on which protease inhibitors you decide to take. These include Rifampin, Rifabutin, Prozac, and Seldane. Side effects reported are headaches, short-term diarrhea, upset stomach, and some rashes; more rarely, kidney stones and blood pressure problems.

Okay, so which protease inhibitors should I keep my eyes on?

There are three protease drugs that are approved. We still do not know if taking these drugs will keep you from getting sick in the long run.

Invirase (Saquinavir) is sold by Hoffman-LaRoche. This drug is the weakest, working only with other antivirals like AZT on a good day. But it causes weaker cross resistance than Norvir or Crixivan.

Norvir (Ritonavir) is made by Abbott. It is absorbed more easily. It appears to be very strong and was approved in February by the FDA for people with advanced HIV disease. It will continue to be in trials with different combinations of nucleosides and protease inhibitors.

Crixivan (Indinavir) is made by Merck. This is also a very strong drug. It was also approved in February by the FDA, has fewer side effect, and may have longer lasting antiviral effect than Ritonavir. **There is a limited supply of Crixivan, so the sooner you sign up the better**. (The PWA health group has a detailed sheet on how to access this drug. Call [212] 255-0520).

Where Can I Get More Information!

Clinical Trials with Protease Inhibitors

√ **AIDS Treatment Data Network**
1-800-734-7104

√ **NIH AIDS/HIV trials hotline**
1-800-TRIALS-A

√ **PWA Health Group**
150 West 26th Street, Suite 201
New York, NY 10001
(212) 255-0520

Patient Assistance Programs/Hotlines

√ **Statlanders Crixivan hotline**
1-800-927-8888
(8:30 a.m.-9:00 p.m.)
Fax: 1-800-238-1549

√ **Abbott's Norvir (Ritonavir) Patient Assistance Program**
1-800-293-4393

Drugs Not To Be Taken With Protease Inhibitors

RITONAVIR (NORVIR*)

Taking ritonavir with certain other drugs may result in serious and/or life-threatening adverse events. DO NOT take ritonavir with any of the following drugs:

	Drug Class	Generic Name	Brand Name
	analgesic	meperidine piroxicam propoxyphene	Demerol Feldene Darvon
	cardiovascular (antiarrhythmic)	amiodarone encainide flecainide propafenone Quinidine	Cordarone Enkaid Tanbicir Rythmol Quinidex, Quiniglute
☞	**antimycobacterial**	rifabutin	Mycobutin
	cardiovascular (calcium channel blocker)	bepridil	Vascor
☞	**cold and allergy** **(antihistamine)**	astemizole terfenadine	Himanal Seldane
	gastrointestinal	cisapride	Populsid
☞	**psychotropic** (antidepressant)	bupropion	Wellbutrin
	psychotropic (neuroleptic)	clozapine	Cozaril
☞	**psychotropic**	alprazolam clorazepate diazepam estazolam flurazepam midazolam triazolam zolpidem	Xanax Tranxene Valium Prosom Dalmane Versed Halcion Ambien

indinavir (Crixivan)

Taking indinavir with certain other drugs may result in serious or life-threatening adverse events. DO NOT take indinavir with any of the following drugs:

	Drug Class	Generic Name	Brand Name
	antacid	cisapride	Propulsid
☞	**cold and allergy (antihistamine)**	astemizole terfenadine	Himanal Seldane
☞	**psychotropic** (sedative/hypnotic)	midazolam triazolam	Versed Halcion

saquinavir (Invirase)

Taking saquinavir with other drugs may result in potentially serious or life-threatening adverse events. DO NOT take saquinavir with any of the following drugs:

	Drug Class	Generic Name	Brand Name
☞	**antituberculosis**	rifampin	Rifadin
☞	**antimycobacterial**	rifabutin	Mycobutin
	antiepileptic	phenobarbital phenytoin carbamazepine	Quadrinal, Mudrane Dilantin Tegretol
☞	**cold and allergy (antihistamine)**	astemizole terfenadine	Himanal Seldane
	corticosteroids	dexamethasone	Decadron

NOTE: The methodology used to identify these drugs was not uniform among the manufacturers.

HOW DO CURRENT DRUGS PERFORM ON VIRAL LOAD TESTS?

Reported Peak Average Reductions in HIV RNA

DRUG OR COMBO	LOG REDUCTION, COPIES OF VIRUS
(Nucleosides)	
AZT alone	.5 log (3 fold) reduction
ddI alone	.5 to .6 log reduction
ddC alone	< .5 log reduction
AZT + ddI	.6 to .8 log reduction
AZT + 3TC	1 to 1.5 log reduction
d4T alone	no data
d4T + ddI	> 2 log reduction *
(Protease Inhibitors)	
Indinavir (alone or combination)	2 to 3 log reduction
Ritonavir (alone or combination)	2 to 3 log reduction
Saquinavir (alone)	<.5 log reduction**
Saquinavir (combination)	.5 to 1 log reduction
Saquinavir high dose	1 to 1.5 reduction*
(Non-Nucleoside RT Inhibitors)	
Nevirapine	> 2 logs reduction ***
Delavirdine	> 2 logs reduction ***

* very preliminary data
** prior to improved formulation
*** maintained for a very short period

Antisense compounds can theoretically be created to interfere with both early and late steps of the viral life cycle. These compounds work a bit like sticking chewing gum in the teeth of a zipper. Antisense is an inverted copy of the RNA which, when it binds to the RNA strands, "gums up" the zipper. GEM 91 (Hybridon) the first antisense compound for HIV is currently in phase I studies. Another, ISIS 5320 (ISIS) is expected to be in clinical studies in 1996. In the lab, antisense products are extremely potent inhibitors of HIV and seem to be less sensitive to the development of resistance.

A preliminary French study of GEM 91 administered single intravenous and subcutaneous doses of the drug and determined that the subcutaneous mode of administration may not be a viable method of administering this drug. Multiple intravenous dose studies are now ongoing, both in France and the US. Laboratory studies of GEM 91 have shown no evidence of resistance in lab cultures after more than 200 days. This is far better than the results seen with nucleoside analogs or protease inhibitors in similar lab studies.

Cellular Targets

Unlike all other antiviral drugs, which target the virus itself, this class of compounds inhibits factors inside the cell which are necessary for viral replication. Attacking cellular targets, instead of targets on the virus itself, offers hope of slowing or avoiding viral resistance because the cellular target does not rapidly mutate like the virus. In general, these drugs work by suppressing compounds inside the cell which the virus needs to complete its reproduction. In the lab, this requires only a small reduction in the level of these compounds, not enough to hurt the cell's own reproductive cycle or function.

Additional Options

Hydroxyurea (Hydrea)

Hydroxyurea is an approved drug used in the treatment of leukemia, inoperable ovarian cancer, and (recently) sickle-cell anemia. Researchers at the National Cancer Institute found that combinations of hydroxyurea and ddI produced a powerful and long-lasting suppression of the reverse transcription step in viral reproduction. Unfortunately, more than a year and half lagged between the initial discovery and the efforts to begin clinical testing. A few initial clinical studies are now underway. Because of this lag time, many people have begun to experiment with hydroxyurea on their own, although virtually no information is available about proper dosing. The dose typically being used, about 1000 mg. per day, is simply guesswork, and might well be too high. Additionally, the lab data suggests that it might be possible or even necessary to use hydroxyurea in an intermittent fashion. Anyone considering off-label use of hydroxyurea should discuss this with a health care provider and carefully monitor health and blood work. The one published lab study says the drug works best in combination with ddI, and there are some reasons it should probably not be combined with AZT (fear of over-lapping side effects). The most common side effect is a mild and reversible bone marrow suppression. In cancer, many people have used this drug for years, even decades. This suggests that its long-term toxicity can be manageable.

Topotecan

Another cancer drug that appears to be able to inhibit HIV through cellular factors is topotecan. This drug is currently in clinical studies as a potential therapy for numerous types of cancers, including Kaposi's Sarcoma (KS) and lymphoma. Studies for KS and HIV-related lymphoma were scheduled to begin in 1995 and anti-HIV activity will also be examined in those studies.

The Future of Antiviral Therapy

The future of antiviral therapy almost certainly will concentrate on the search for rational combinations of new and existing drugs. While there is little reason to expect that any single drug will be both potent and have long term activity without encountering resistance, there is already good reason to expect that some combinations will produce this effect. The success of combining AZT and 3TC demonstrates that the right combinations can be better than the sum of its parts. Most researchers expect to see even better results when we begin to combine potent drugs which have different mechanisms of action and different patterns of resistance.

Other antiviral approaches that are being pursued include **glucosidase inhibitors** (inhibits the sugar coating of HIV), a synthetic formulation of **bitter melon** (multiple mechanisms of action), **cyclophilin inhibitors** (inhibits fusion of infected and uninfected cells), **tat inhibitor and ribozymes** (gene therapy) directed against HIV.

Additionally, there are immune-based antiviral approaches such as **tumor necrosis factor (TNF) inhibitors, HIV-specific cytotoxic T-lymphocytes (CTL) expansion and HIV specific monoclonal antibodies.**

We already know from the early study of protease inhibitors that a larger degree of antiviral suppression results in a larger degree of CD4+ cell improvement. These data also suggest that this will result in larger clinical improvements as well, although only longer studies can prove this point. The benefits we all hope to see from better and longer-lasting combinations should produce results far beyond any achieved to date. This new hope will be further increased as still other drugs, attacking other viral targets, become reality in clinical testing. This includes the new class of compounds known as integrase inhibitors, wider use of antisense and gene therapy. As well as improved versions of existing drugs.

Conclusion

The principal unanswered question is whether, in the face of near perfect viral suppression, the immune system will be capable of restoring itself. The data are not yet clear on this point, though the recent evidence from protease inhibitor studies has encouraged a great number of researchers on this point.

A final question is whether it will be possible (or necessary) to maintain high levels of viral suppression for a person's entire lifetime. On this point, scientists are divided. Some believe it may be possible to eventually conquer the infection completely, while others dispute this. If this isn't possible, the challenge of maintaining the use of potent antiviral medications for decades will be difficult, but certainly not impossible.

At the very least, it is fair to say that the new generation of antiviral drugs and their combinations is bringing on a new era of new hope in the fight against HIV/AIDS.

Immune Therapy 20

Immune-based therapies are directed at strengthening the severely damaged immune system and to assist in destroying the virus in HIV infected individuals.

Interleukin-2 (IL-2)

Interleukin are cell-to-cell hormones which help to activate the immune system. IL-2 is normally made in CD4+ T-cells. IL-2 allows T-cells to divide and to produce other hormones to activate other immune cells. Overall, IL-2 increases the number of T cells that are able to recognize foreign proteins and also activates CD8+ T cells which kill cells infected by viruses. IL-2 also activates B cells which make antibodies in HIV disease. IL-2 production is decreased and defective in those with HIV infection. Studies have been done to evaluate replacing IL-2 in HIV infected individuals.

- In combination with AZT, IL-2 was found to:
  -increase natural killer cell activity (natural killer cells function to kill infected cells).
  -improve delayed hypersensitivity reactivity (test of T-cell function).

- In another study, AZT and IL-2 were compared to AZT alone. The combination demonstrated:
  -increase in CD4+ cells.
  -improved natural killer (NK) cell activity
  -Due to its extremely high cost and potential side effects, much more study needs to be done to evaluate the role of IL-2 in HIV disease therapy.

Interferon Alpha

Interferons are cell-to-cell hormones that fight viruses living inside cells. Alpha interferon is produced mainly by immune cells called mononuclear phagocytes. Currently, recombinant interferon alpha is being used to slow the progression of Kaposi's sarcoma in AIDS.

Oral interferon (taken by mouth) has been evaluated in chemical studies and has no beneficial effects in disease. Currently, studies are being done to evaluate the combination of AZT and interferon alpha. Cost and the development of resistance to interferon are the main obstacles in the use of interferon alpha. Alpha interferon often causes flu-like symptoms when taken by injection. Another major side effect of AZT in combination with interferon alpha is neutropenia (lowering of a type of white blood cell called neutrophils which fight bacterial infections).

Hyper-immune Globulin

These are antibodies which are developed in pigs or harvested from HIV+ individuals in the early stage of infection. One study demonstrated positive changes in T cells and improvement in diarrhea, fever, and neurologic damage. Expense and serious side effects may limit the possible use of this hyper-immune globulin.

Gene Therapy:

Gene therapy is the introduction of new genetic material into of a person resulting in a therapeutic benefit. Problems in research involve finding appropriate target cells, finding a method to introduce the genetic material into the cells and finding genetic material that will inhibit the HIV life cycle. Gene therapy holds exciting promise but is still in its infancy. Some clinical trials have begun, but it will take many years to perfect the treatments.

Thymic Peptides (Timunox, Thymopentin, Leucotrofina)

The thymus is a gland in the body where immature T cells are defined and programmed to recognize self versus non-self. Preliminary information shows reduced disease progression in asymptomatic patients. The most effective route for administration is injection but Leucotrofina is an oral preparation. These can be obtained either from clinical studies or some AIDS buyer's clubs.

Anti-Tumor Necrosis Factor Agents

Pentoxyifylline (Trental):

Levels of a messenger hormone called tumor necrosis factor (TNF) are often elevated in HIV disease. These high levels are usually seen in those with weight loss and wasting. Pentoxyifylline was shown to decrease tumor necrosis factor levels. Clinical correlates are currently being evaluated.

N-Acetyl Cysteine (NAC):

NAC increases levels of glutathione, a natural antioxidant which is very low in advanced HIV disease. NAC also decreases levels of tumor necrosis factor. It is not well absorbed and should be taken with vitamin C to increase absorption

Antioxidants

(Vitamins E, C, and beta carotene; NAC, thioctic acid, quercitin, melatonin):

These substances occur naturally in the body or are found in many fruits and vegetables. One clinical study demonstrated that beta carotene supplements help to maintain CD4+ T-cell counts. These supplements are available without a prescription and available at all drug and health food stores.

Vaccines

The major goal of vaccine development is to develop a vaccine which prevents non-HIV infected individuals from developing HIV infection when exposed to the virus.

In those already infected with HIV, vaccines may boost the immune system which may prevent further spread of the virus and help to clear infected cells in the body.

The major problem facing vaccine research is finding a safe and effective vaccine for a virus which is constantly mutating and, therefore, becoming resistant.

Salk Vaccine (Immunogen):

This vaccine is made from inactivated HIV and injected over months to years. Three studies have shown improvement in T cell function (measured as delayed type hypersensitivity responses). One study indicated that vaccinated patients had fewer, opportunistic infections, and fewer deaths.

Gene Tech GP-120:

This vaccine demonstrated improvements in both major components of the immune system. The goal of vaccines is to stimulate the immune system. Injecting components of HIV (GP-120, GP-160 and others) stimulates the immune system to make antibodies which are produced by B cells.

Most studies have shown that antibodies are produced only for a few months after the vaccine is given. Future research must find the portion of HIV which produces the most sustained responses.

Vaccines will most likely need to be given multiple times. The time interval between doses much be elaborated.

FOOTNOTES

1 by Robert Rockwell, M.D.
March 1994

2 Treatment Strategy, April 1996
Project Inform Discussion Paper #1

3 Robert Rockwell, M.D., March 1995

4 Compiled and updated February 1996
from excerpted writings of Karen Ivester, R.N., Dave Wagner, J.D., and Robert Rockwell, M.D.

5 by Jeff Graham, February 1996, updated 9/96

6 Developed by the International AIDS Society, first published by *Nature Medicine*, June 1996

7 by Robert Dunning, Jr., R.N.., M.N., C.S.
November 1995, updated by Eric D. White, September 1996

8 by Robert Rockwell, M.D., May 1995, updated 9/96

9 Project Inform Fact Sheet, 12/13/95

10 *Positively Aware,* September/October 1996

11 Project Inform Fact Sheet, 12/13/95

12 AIDS Treatment Data Network, 8/27/96
For more information about treatments contact the Network at (800) 734-7104.
E-mail address: atdn@aidsnyc.org

13 Project Inform Fact Sheet, 12/13/95

14 by Lawrence M. Prescott, Ph.D., *Positively Aware,* September/October 1996

15 Project Inform Fact Sheet, 12/13/95

16 by Martin Delaney, Founding Director of Project Inform, San Francisco, CA.
For more information, contact the Project Inform Hotline, 800-822-7422 or the Project Inform World Wide Web service: http://www.projinf.org)

17 Excerpted from *Protease Inhibitors: How to use them the right way.*
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18 copyright BETA (Bulletin of Experimental Treatment for AIDS) Published by the San Francisco AIDS Foundation (July 1996)
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19 Project Inform Fact Sheet, 12/13/95

20 Robert Rockwell, M.D., May 1995

This section updated by Dave Wagner, J.D, May 1995.

Updated and revised by Robert Dunning, Jr., R.N., M.N., C.S., January 1996 and Alicia A. Culver, June 1996

This section reviewed, revised and updated September 1996 by Alicia A. Culver with input from Eric D. White, AIDS Survival Project Treatment Resource Specialist, Wayne Deal, R. Ph., Patients Pharmacy and William Ramirez, M.D.
Thank you!

NOTES

What's the difference between 1&2?

1. Nucleoside Analogues Reverse Transcriptase Inhibitors
2. Non-Nucleoside Analogues Reverse Transcriptase Inhibitors
3. Protease Inhibitors (Does this have a name like the others?)

Are PI's nucleoside analogues? non-nucleoside anal

Do you take 1, 2 & 3 together?

usually → 2 RTI's + 1 PT or 1 RTI & 1 PT } take what you can take

↑ both 1 or 2 or a combo?

→ don't combine PI's → doses are questionable

Are there integrase inhibitors?

analogue - chemically looks like something else

WOMEN & HIV

ABOUT WOMEN & HIV 1

Women account for about 12% of all AIDS cases in the United States and 50% worldwide. Furthermore women are being infected at a rate greater than any other population. However, HIV is still under diagnosed and under researched in women. This is in part because many women in the United States are not perceived to be "at risk" and often physicians do not recognize early signs of HIV infection in women. Although treatment and care issues are similar for both men and women, certain issues concerning HIV treatment are specific to women. *Guidelines for Women with HIV/AIDS* will address some of these issues, including social, psychological, and physical issues of HIV and women.

SOCIAL

FAMILY/FRIENDS

Unfortunately, there is no "Guide to the Emotional Management of HIV"- no "right" or "wrong" way to tell someone you're positive. Relationships may change as people become aware of your HIV infection. Although revealing your HIV status may pose the risk of rejection by some people, "coming out" can also strengthen relationships and open the door to new ones. It is important to identify a network of family and friends with whom you can openly discuss HIV and address the unique concerns that come with the virus. (*Operation: Survive! Committee's Note: At the end of this section is a list of organizations that provide services specifically for women).*

PARTNER/LOVER

It is most important to inform your lover or spouse of your HIV infection, as it also has an impact on him or her. Although knowledge of your HIV status can certainly disrupt a good relationship, don't assume it will destroy one. Finding an appropriate time or method to tell your partner that you have HIV is difficult and will of course vary with each situation. It may be helpful to provide him or her with printed information to better understand the disease , as well as information on where he or she can seek anonymous HIV testing. Perhaps seek out a support group so that you and your partner will be able to meet other couples that are sharing similar concerns regarding HIV and relationships. If you're in an abusive or threatening relationship, it would be a good idea to consult first with your local AIDS organization and battered women's center. If not currently in a relationship (but wish you were), don't assume that HIV means you can no longer give and receive love. Although sex may not be your top priority at this time, it is important to remember that sex is something which can help affirm life. *(Operation: Survive! Committee's Note: Safer sex practices are discussed in the Safer Sex section of this workbook).*

CHILDREN

In addition to discussing HIV with your lover, you also should consider informing your children of your HIV status. Children are very perceptive and often know (although they may not have been told) that something is wrong, and may think that your illness or stress is their fault. Reassure them that they are not the cause. Honesty may be the best approach in telling your children that you have HIV, yet remember to provide information to them at an

educational and developmental level they can understand. For example, a very young child won't understand that fatigue often accompanies HIV, but would accept that sometimes mom's get sick or tired and need to take naps, just like little kids. Upon learning that their mother is infected with HIV, older children often experience anger or frustration. Unfortunately, few special services are available to address their special needs. It may help to find someone, such as a social worker, family member, special teacher, or therapist with whom your children can talk freely. Acknowledge that you and your doctor do not have all the answers concerning HIV, but as you learn more you will explain more to them.

Unfortunately, many women discover their HIV status during pregnancy or when a child is diagnosed HIV+. In the case of an HIV+ child, it is even more important to be honest. A child knows if he or she is different than other children. . Further considerations regarding pregnancy and parenting can been found later in section.

Psychological

Just as it is important that you address the ways in which your HIV infection can affect your relationship with others. It is equally important to address the ways in which HIV affects your relationship with yourself. First, last and always remember that guilt, blame or shame accomplish nothing. Nobody asks for HIV anymore than they beg for a car wreck. Certainly your life has been physically and emotionally assaulted, but not necessarily beyond repair.

Support Groups and Community Based Organizations

Support groups and community organizations can provide you with the opportunity to learn more about the disease while allowing you to learn the ways in which others are dealing with similar problems. Being among women (and men) with some of the same concerns as yourself provides the feeling that you are not alone in facing this disease, and can lead to valuable friendships. Also, studies have shown that support groups can actually have "clinical benefit," helping to delay the onset of disease. The extent of participation and sharing is entirely up to you and you should never feel that you are being forced to participate in anything that makes you feel uncomfortable. For a list of support groups, contact an AIDS organization in your area. A list of other resources for women is located at the end of this fact sheet.

Stress Management

Having a life-threatening disease naturally will produce stress. However, since stress can adversely affect your immune system, controlling it plays a key role in controlling HIV. So anticipate and learn the skills needed to handle stress and to help keep it from affecting your health.

Try to identify the symptoms of stress, both physical and mental such as muscle pain and depression.

Find out what you believe is the source of the stress. In many situations (such as finding out you have HIV) anxiety is a very natural reaction.

Sometimes, it may be possible to prevent the stress through problem solving methods, changing the environment that causes the stress, or simply avoiding the stressful situation altogether (without avoiding life altogether).

Since no one can avoid all stress, finding ways in which to manage your stress is beneficial. Some suggestions include: exercise, yoga, massage, meditation, support groups, network of family and friends with whom you can talk, and therapy.

Physical

Women with AIDS experience many of the same infections as men. Unfortunately, many women do not access the information needed to extend their lives some of it as simple as an inexpensive antibiotic which can prevent PCP (pneumonia). In addition to the women specific information included here, we encourage you to seek out general treatment information and find a sensitive and knowledgeable doctor who will work with you to develop a personal treatment strategy.

Idiopathic Thrombocytopenia (ITP)

ITP is an abnormally low platelet count common in people with HIV as well as intravenous drug users. Anecdotal data suggests it is particularly common in IV drug users who are women. Symptoms include: easy bruising, bleeding in the mouth and gums (more than usual), rectal bleeding, and/or blood in vaginal secretions (non-menstrual). If your platelet count falls below 25,000/mm3, continue to monitor your platelet count closely and/or began therapy. Sometimes platelet counts will return to normal levels without therapy. A definitive standard-of-care has yet to be established but some options include: IVIG (immunoglobulin), high dose AZT, short term corticosteroids, Vitamin C, interferon, Dapsone, or (as a last resort) removal of the spleen. Unfortunately, the results of most ITP therapies are temporary. Avoid drugs that interfere with platelet formation such as aspirin, anti-inflammatory agents (i.e.: Advil, Motrin, Naprosyn), and alcohol.

Menstrual Abnormalities

Little research has documented the relationship between HIV and menstruation or hormone production. Anecdotally, HIV+ women report an increase in menstrual irregularities including hypermenorrhea (increased blood flow), amenorrhea (decreased flow or missed periods dymenorrhea (cramps), and increased Pre-Menstrual Syndrome (PMS). Researchers are not certain whether irregularities are due to hormonal changes relating to HIV infection or side effects of the drugs being used to combat the infection. A recent study comparing asymptomatic HIV positive women to HIV negative women did not reveal any significant differences in either hypermenorrhea or dysmenorrhea. Regardless of the scientific research (or lack of) if you are experiencing menstrual problems consult your health care provider for diagnosis and treatment. Hypermenorrhea can lead to anemia, while amenorrhea could suggest an unplanned pregnancy, ovarian cysts, or in some cases early menopause. Dysmenorrhea could indicate Endometriosis, an infection in the lining of the uterus, which left untreated can lead to more serious problems. Medications useful for relief of cramps are now available over-the counter (OTC) . They include: Ibuprofen (Motrin, Advil, or much less expensive generic versions) and Naproxyn Sodium (Aleve). These medications are not recommended for some women (see ITP) and if taken improperly (on an empty stomach or at high doses) may cause stomach problems or liver damage. Although no clinical data exist, many women have suggested a variety of alternative treatments. Certain herbs and roots including common ginger root) may help relieve cramps or PMS and are readily available through health food stores and some pharmacies. Remember that herbs and other natural medications are still medications. Follow package or practitioners instructions as you would any other medication. Other suggestions include: a heating pad, yoga (lie in a "fetal" position on your back), or an orgasm. For women who are not in drug-abuse recovery,

medical use of marijuana may be an option. Since everyone is different. experiment with various medications and/or alternative treatments to find what works best for you. If needed, ask your physician for stronger medication. Many women have found that reducing caffeine and salt intake is helpful with PMS.

Regular Gynecological Exams and Cervical Cancer

In 1993, 13,500 new cases of cervical cancer occurred among women in the United States. Approximately 4,400 women died from cervical cancer. Furthermore, a higher incidence of invasive cervical cancer has been observed in HIV positive women compared to HIV negative women. Although the overall 5-year survival rate for all cervical cancer is 66%, the survival rate for cancers detected and treated early is 100%! Anecdotal data suggest that cervical dysplasia (abnormal changes in the tissues covering the cervix, a pre-cancerous condition) appears to progress more quickly in HIV positive women, especially those who are severely immune compromised. An observational study in New York compared pap results of HIV positive pregnant women with those of a matched group of uninfected pregnant women. A larger percentage of women with <200 CD4+ cells had cervical dysplasia, while positive women with >500 CD4+ cells displayed rates of cervical dysplasia similar to that of the negative women. **It is vitally important that positive women have regular exams and pap smears.**

A pap smear involves scraping some cells from a woman's cervix and smearing them on a slide. The slide is then observed under a microscope. Government programs can help pay for yearly exams: check with your local health department. "Abnormal pap results are graded numerically as CIN 1, 2 or, 3 representing increasing progression of dysplasia to involve deeper layers of the cervical tissue. CIN stands for Cervical Intraepithelial Neoplasia.

The higher the number is, the greater the risk of it developing into cancer. If your pap smear is found to be abnormal. you should be referred for a colposcopy (colpo) exam. During a colposcopy, your doctor actually views the pattern of cells on the cervix using a colposcope (a kind of microscope with a strong light that magnifies the cells on the cervix). If anything unusual is seen, a small piece of cervical tissue will be removed (biopsy). In addition to a strong "pinching" feeling, the biopsy may cause some pain similar to menstrual cramps.

In a recent study of 52 HIV positive women, in which all had both paps and colposcopy exams performed, cervical dysplasia was detected by pap smear in 35% of the women. Colposcopy revealed dysplasia in 50% of the women. Early reports from another study have suggested equal sensitivity between pap and colposcopy when paps are performed and read properly. This same study hopes to determine if some positive women should have pap smears done more often than others. Most gynecologists would agree that a colposcopy is the preferred diagnostic tool. However, a colpo is an expensive and more invasive procedure which may not be necessary if you have regular and consistently normal pap smears. Although pros and cons of pap versus colpo are still being debated, and no specific recommendations have been issued: all agree that at the very least HIV positive women should have a pap smear every 12 month (many say 6 months). A baseline colposcopy followed with regular paps may be wise if you have a history of an abnormal pap, have been diagnosed with Human Papilloma Virus (HPV), or have <200 CD4+ cells. Another option for this subgroup of positive women would be more frequent pap smears. It is generally accepted that HPV can lead to cancer. Furthermore, many women with vaginal HPV will also test positive for anal HPV. Therefore, if you have been diagnosed with HPV, get it treated early and suggest that your gynecologist also perform an anal pap smear.

Treatment of cervical cancer or cervical dysplasia will vary depending on the severity of the problem. Cryosurgery is the most common and involves freezing the top layer of cervical skin with liquid nitrogen. By destroying the top layers of skin in this manner, it is hoped that new healthy skin will grow back. Cryosurgery will also probably cause cramping. If the cancer is more advanced, it may require laser surgery, burning the skin, radiation, chemotherapy, or surgery.

Pelvic Inflammatory Disease (PID)

PID is usually caused by untreated sexually transmitted infections, such as chlamydia and gonorrhea. Often early symptoms are ignored and PID is not diagnosed until an advanced stage. PID can cause tubal scarring leading to infertility or ectopic (tubal) pregnancy. The most common symptom is pain ranging from moderate to intense in the lower abdomen. Additional symptoms may include: fever, cervical tenderness and/or abnormal vaginal discharge. Blood work which may suggest PID include: elevated erythrocyte sedimentation rate and elevated C-reactive protein. A positive lab result for Gonorrhea or Chlamydia combined with symptoms would confirm a diagnosis of PID. Other diagnostic methods include: pelvic exam, sonogram (using sound waves to create an image of internal organs), or laparoscopic examination (a surgical procedure in which a small microscope is inserted through an incision in the lower abdomen; often performed as outpatient) .

Hospitalization is recommended for treatment of PID in HIV+ women although mild or early infections might be treated on an outpatient basis. HIV+ pregnant women suspected of PID should be hospitalized, treated IV with antibiotics approved for use during pregnancy, and monitored closely. Many antibiotics used to treat PID are contraindicated (not recommended) for use during pregnancy. Below are treatment options for non-pregnant women (after first treating the original cause of the infection):

Antibiotic Regimen A:
Cefoxitin (2g IV q 6 hr) or Cefotetan (2g IV q 12 hr) PLUS Doxyclycline (100mg IV or PO q 12 hr). Continue therapy at least 48 hours after improvement.

Antibiotic Regimen B:
Clindamycin (900mg IV q 8 hr) **PLUS** Gentamicin (loading dose IV or IM 2mg/kg) followed with Gentamicin (mx dose 1.5mg/kg q 8 hr)

In very severe cases a hysterectomy may be recommended. A hysterectomy involves removal of all or part of the reproductive organs. As with any major surgery, complications could arise. The risk of complications may be heightened by HIV infection. A second opinion is advised whenever major surgery is being considered.

Vaginal Infections

Vaginal infections, especially yeast infections: are common and will usually respond to standard therapies. However, with a compromised immune system you may notice infections which don't respond as well to topical treatments and require more aggressive therapy. As well, if exposed to an STD you could experience a more serious infection especially if left untreated. Consult (Guidelines for Management of GYN Infections) for more information and remain diligent in preventing STD.

PREGNANCY 2

Making Difficult Decisions

One important choice that arises with many HIV-infected women, is whether or not to have a child and what (if any) intervention should be used to reduce the risk of transmission from mother to-child. Several factors need to be considered when making these decisions or when counseling a woman who is making these decisions.

Without treatment or intervention, in the United States, there is an average 20%-30% chance of transmitting the virus to the fetus during pregnancy, labor, or delivery.

The possibility of transmitting HIV to a child also exists through breast feeding. Therefore, HIV+ women in developed countries such as the United States are advised against breast-feeding.

If a woman's overall health is very poor or she does not receive adequate prenatal care, the risk of transmission could be much higher and possibly place an increased strain on her health.

Factors involved in perinatal transmission of HIV are not fully understood. A high level of virus in the mother's bloodstream or a deficiency in Vitamin A may predict an increased risk of mother-to-baby transmission.

Who will care for the child if mom becomes ill and can no longer do so? Some states allow joint guardianship between the parent and a future or temporary guardian. A responsible and caring mother should never feel pressured into giving up her child unwillingly or prematurely. Refusal of treatment or the decision to continue a pregnancy does not legally constitute irresponsible behavior. Local AIDS organizations can usually provide legal advise or a referral.

Many medications used to treat HIV-related infections either have not been studied in pregnant women or are contraindicated for use during pregnancy. Pregnant HIV+ women should seek prenatal care with an obstetrician familiar with HIV and willing to consult with her primary care practitioner. Special Medicare guidelines expand income restrictions, allowing temporary coverage for prenatal, delivery and postpartum care for women who otherwise could not qualify. Often providers at government funded clinics are very knowledgeable in HIV and offer affordable care. **Ultimately decisions about pregnancy must be made by each individual woman.**

It has been assumed that a low CD4+ lymphocyte (T-cell) count may be a risk factor in perinatal transmission. However, more recent observations suggest otherwise. In ACTG-076, women who had around 200 CD4+ cells were no more likely to transmit than women with CD4+ counts much higher. In addition, some prenatal care providers have noticed that CD4+ counts don't indicate as much as CD4%. At time of this printing, no controlled studies have been performed to confirm these observations. A woman's immune system (regardless of HIV status) is naturally suppressed during pregnancy and then rebounds (returns to normal) after birth. It was initially feared that since an HIV+ mother's CD4+ count doesn't always rebound to the pre-pregnancy level, that pregnancy could be dangerous for positive women. However, recent studies have shown that pregnancy does not seem to adversely affect an HIV+ woman's health or cause her disease to progress more quickly.

PERINATAL TRANSMISSION RESEARCH 3

Data from study ACTG 076 revealed a significant reduction in the percentage of infected babies born to healthy HIV+ women who took AZT on a specific regimen. The women all had CD4+ counts above 200, with the highest CD4+ count at 1800. They took the drug orally (by mouth) during the last half of their pregnancy and were given infusions during labor and delivery. Their babies were given oral AZT for 6 weeks. Among the group of women who took AZT, approximately 8% of the babies were infected. In the placebo group (women who did not take AZT, the rate of transmission was about 25%. Researchers are unclear as to whether AZT reduced the mother's level of virus and therefore prevented transmission or whether there is something special about the molecular make-up of AZT which reduced transmission. Another unknown is the long term affect on those children given AZT as a fetus and at birth. Although no obvious defects or immediate side effects have been reported, the children who (as fetuses) participated in this study will be followed until age 21.

The Department of Health and Human Services recently issued guidelines regarding the use of AZT to reduce perinatal transmission and can be found in the August 5. 1994 issue of the CDC's Morbidity and Mortality Weekly Report (MMWR) *(Available in the Treatment Resource Center at AIDS Survival Project).* The Centers for Disease Control (CDC) also issued guidelines regarding testing of pregnant women for HIV. Both sets of guidelines strongly emphasize the woman making an informed decision with input and advise from her physician.

Another study (ACTG 185). will consider a less healthy population of pregnant women already taking AZT. Women and babies in this study will take AZT as in ACTG 076 with the addition of either Hyper-Immune Globulin (HIVIG) or regular Immune Globulin (IVIG). A smaller study nested within this one will ask whether AZT resistant virus is being transmitted from mother to child and how this may affect the health of the child. An observational study (not administering drug, just looking at lab variables, etc.) of pregnant HIV+ women being conducted by the Ariel Project (Pediatric AIDS Foundation) should provide additional insight into perinatal transmission of HIV.

WHAT IF YOUR CHILD IS POSITIVE?

When a child is born, she or he will still carry the mother's HIV antibodies and therefore may test false positive. Children usually lose their mother s antibodies by 18 months and you can usually get an accurate antibody test result after your child's 18th month. However, other lab tests (HIV culture and Polymerase Chain Reaction or PCR) can provide a diagnosis much sooner. In the case that your baby is HIV+, she or he will require a great deal of special care.

Several factors must be considered if your baby is positive. HIV+ babies usually have a higher rate of health problems, develop mental difficulties, and more severe childhood diseases. Caring for a sick child should not cause you to ignore your own health. Remember that as important as insuring your child a healthy happy life may be, it is equally important they have a healthy mom.

POTENTIAL INDICATORS OF HIV INFECTION IN WOMEN

Gynecological Infections

These conditions may occur with increased severity and/or frequency and be more resistant to therapy in women with HIV:

Vulvo–Vaginal Candidiasis (VVC)

Pelvic Inflammatory Disease (PID)

Human Papilloma Virus (HPV)

Cervical Dysplasia/Neoplasia

Herpes Simplex Virus (HSV)

STD & HIV Interactions

- Locally, STDS, both genital ulcers and nonulcerating STDs such as cervicitis, allow penetration of HIV through lesions that disrupt the integrity of the genital epithelium, increasing the woman's susceptibility to HIV transmission.

- Atypical STDs (eg. facial molluscum) and recurrent STDs may indicate immunosuppression due to HIV infection.

Routine Pelvic Exam should include:

- ♀ Pap test
- ♀ Chlamydia and gonorrhea assay
- ♀ Wet mount and KOH prep of any cervical or vaginal discharge
- ♀ Serum RPR

Guide to the Management of GYN Infections in Women with HIV/AIDS

Infection	Symptoms of Active Infection	Diagnostic (Dx) Procedures	Treatment (Tx) for Active Infection
Chancroid *(H. ducreyi)* bacterial infection	Painful vaginal ulcers, with no evidence of HSV (herpes simplex virus) or *T. Pallidum* (syphilis) infection. Inflammation of lymph glands in the groin area (inguinal adenopathy) is also seen in approximately 1/3 of patients.	Diagnosis is made by clinical observation of symptoms and testing to eliminate the possibility of syphilis or herpes. Definitive dx requires identification of H. ducreyi in special culture media not readily available. If the dx is unclear, doctor may also recommend treatment for syphilis.	Azithromycin (1g PO 1x), Ceftriaxone (250mg IM 1x), Erythromycin (500mg PO 4x day x 1wk). Alternatives: Amoxicillin (500mg plus 125mg clavulanic acid PO TID x 1wk) or Ciprofloxacin (500mg PO BID x 3 days).
Chlamydia *(C. Trachomatis)* **and Gonorrhea** *(N. gonorrhoeae)* bacterial infections	Chlamydia infection is very common, especially among young adults. Most women will not experience any symptoms. IF you do, they may include: vaginal discharge, spotting following intercourse or between periods, lower abdominal pain, salpingitis (inflammation of the Fallopian tubes). Gonococcal infections (gonorrhea) among women usually produce no symptoms and HIV+ women at any risk of this STD should be tested on a regular basis. Co-infection with gonorrhea and chlamydia is common and often leads to PID.	Pelvic exam (involves the application of pressure to the outside of the lower abdomen to detect enlarged tubes or tender and hot abscesses) and sample of discharge for microscopic evaluation for *C. trachomatis*. *N. Gonorrhoeae* is diagnosed by culturing a sample of a vaginal discharge.	Chlamydia: Doxycycline (100mg PO BID x 1 wk). Azithromycin (1g PO 1x). Alternatives: Ofloxacin (300mg PO BID x 1 wk), Erythromycin base (500mg PO 4x/day x 1 wk), Erythromycin ethylsuccinate (800mg PO 4x/day x 1 wk), Sulfisoxazole (500mg PO 4x/day x 10 days). Many antibiotics are safe and effective for treating uncomplicated gonorrhea. Recommended: Ceftriaxone (125mg IM 1x), Cefixime (400mg PO 1x), Ciprofloxacin (500mg PO 1x), Ofloxacin (400mg PO 1x) PLUS Doxycycline if chlamydial co-infection is suspected. *See "drug Interactions" for Tx during pregnancy.*
Herpes Simplex Virus (HSV) viral infection	Oral infection (HSV-1): blisters on lips, tongue, or cheek, fever, swollen lymph nodes in neck. Genital infection (HSV-2): All or some of the following: painful blisters in/around vagina, rectum, and/or anus, painful urination, genital irritation, fever, headaches, muscle aches, malaise. *Note: Some may experience symptoms only once. Many persons will, however, experience recurrent episodes.*	See your medical provider as soon as possible. S/he will try to culture HSV from fluid of one of the blisters for an accurate diagnosis. Can sometimes be diagnosed by visual exam.	The optimal acyclovir dosage for HIV+ patients is being debated. Experience suggests 400mg PO 3-5x/day until blisters are completely gone. For a very severe outbreak, IV acyclovir may be required (5mg/kg of body weight, q 8 hrs). For acyclovir resistant dz: Foscarnet (40mg/kg IV q 8 hr x 14 days). *Other therapies are being researched for acyclovir-resistant herpes.*
Genital Warts/ Human Papilloma Virus (HPV) viral infection	Multiple tiny white spots (warts) on vagina or around anus, soft whitish tumors with fine finger-like projections. Less frequent: vaginal discharge, bleeding after intercourse. Recent studies suggest that women who have vaginal HPV often also have anal HPV. Warts can lead to cervical cancer, and should be taken seriously.	Colposcopy (an instrument called a colposcope is used to magnify the cervix so that a biopsy can be taken of any warts seen), pap smear (cells brushed or scraped from cervix). External genital/perianal warts can be diagnosed visually by soaking the skin in area with vinegar or 3% acetic acid for 5 minutes and then examining the skin directly. An anal pap smear is also advised.	*Consult your GYN provider for exact Tx regimens which may include one or more of the following:* Cryotherapy (cryo) with liquid nitrogen or cryosurgery (cryosurgery recommended for internal warts only), Podofilox 0.5%, Podophyllin 10%-25%, Trichloroacetic acid (TCA) 80%-90%, or Electrodesiccation (low level electricity "burns" the wart). Cervical warts: always be checked for cervical dysplasia. Surgical removal may be recommended for anal or vaginal warts. Some doctors utilize laser surgery. *Note: Other Tx are being studied.*
Syphilis bacterial infection	Primary syphilis: hard, red sores around genitals, anus, or mouth. Secondary syphilis: mucous patches in genitals, skin rashes, fever, weight loss, headaches, hair loss. Neurosyphilis: headaches, memory loss, confusion. Can be easily be mistaken for AIDS related neurologic disorders. Has been observed in people with HIV during primary and/or secondary syphilis. *Note: many women may not experience symptoms.*	A blood test (RPR or VDRL) drawn at least 7 days after ulcers appear is normally used. Abnormal blood results have been observed among HIV+ patients (unusually high, low or fluctuating titers), so your doctor may recommend a biopsy be taken of one of the sores for microscopic examination. Syphilis is often found in the cerebral spinal fluid (CSF) of HIV+ patients with primary or secondary syphilis infection and could affect the central nervous system (CNS). Your doctor may also want to check the CSF by lumbar puncture (a thin needle is inserted into the spine and fluid is withdrawn).	Benzathine penicillin G 2.4 million units administered IM is preferred Tx. Some experts recommend additional Tx, such as multiple doses (2.4 million units, 1 dose a week for 21 days, IM) or other antibiotics in addition to benzathine penicillin. If patient is allergic to penicillin, she may be desensitized (by administering gradually increasing doses), then treated with regular adult penicillin regimen (a minimum 6-12 month follow up is recommended). If penicillin doesn't work: Doxycycline, (100 mg PO BID) or Tetracycline (500 mg PO 4x/day) but are not found to be as effective as penicillin.
Vaginal Candidiasis fungal infection	Creamy white or yellow discharge accompanied by itching or burning while urinating, raised gray and white patches on vagina. *Note: Similar symptoms could indicate other vaginal infections: vaginitis, bacterial vaginosis, or trichomoniasis. Consult your doctor for absolute diagnosis.*	Often by observation. A sample of the discharge should be taken for microscopic examination and other causes, such as chlamydia, should be considered.	Nonprescription meds (OTC, over-the-counter): Gynelotrimin, Monostat 7, etc. Stronger treatments if OTC treatments are not effective: clotrimazole, ketaconazole, itraconazole, or fluconazole, applied intravaginally (creams or suppositories used inside the vagina) or systemically (pills taken orally) as monotherapy or in combination.

Legend: **IV** = intravenously **IM** = intramuscularly **PO** = by mouth **TID** = 3 times a day

Guide to the Management of GYN Infections in Women with HIV/AIDS

Prophylaxis (Px) and Maintenance (Mx) Options	Possible Side Effects from Treatment	Drug Interactions
Px: Avoid infection or reinfection by using condoms. It is best to avoid sex while infected to help the sores heal. Mx: Follow-up in 3-7 days with additional follow-up if not beginning to heal by 7 days. If unable to follow-up, the single dose azithromycin or ceftriazone is NOT recommended..	Erythromycin: upper abdominal pain, nausea, vomiting, diarrhea, hepatitis. Amoxicillin: nausea, vomiting, diarrhea. Antibiotics often cause yeast infections. See candidiasis prophylaxis.	Erythromycin: inhibits metabolism of therapeutic agents, particularly theophylline, carbamazepine, digoxin, warfarin, and oral contraceptives. Concurrent use of erythromycin and theophylline may increase theophylline serum levels. *Ciprofloxacin should not be used during pregnancy.*
Px for newborns: Erythromycin (0.5%) ophthalmic ointment applied topically, one time. Or tetracycline (1%) ophthalmic ointment applied topically, one time. Px for adults: Avoid new infections or reinfection by using condoms.	Azithromycin: gastrointestinal disorders. Erythromycin: see chancroid. Tetracycline: nausea, vomiting, anorexia, skin rashes. Doxycycline: same effects as tetracycline. Antibiotics often cause yeast infections. See candidiasis prophylaxis.	Azithromycin with antacids: decreased azithromycin absorption, so administer these drugs at least 2 hrs. apart. *Recommended Tx for Chlamydia during PREGNANCY: Erythromycin base (500mg PO 4x/day x 1 wk). Alternatives: Erythromycin base (250mg PO 4 x day x 2 wks), Erythromycin ethylsuccinate (800mg PO 4x/day x 1 wk), or if Erythromycin cannot be tolerated, Amoxicillin (500mg PO TID x 1 wk). Gonorrhea Tx recommended during PREGNANCY: Cefuroxime axetil* (1gm PO 1x) PLUS *Erythromycin or Amoxicillin if coinfection exists. Women who cannot tolerate Cefuroxime should receive Spectinomycin* (2g IM 1x).
Mx: Acyclovir (200mg PO 3-5x day) Px: Use condoms to avoid exposure of partner or re-exposure to yourself. "Shedding of virus" and transmission of HSV has been documented to occur without ANY physical evidence of an outbreak.	Acyclovir: Most people tolerate acyclovir extremely well. If side effects are noticed, they may include: dizziness, headaches, nausea, diarrhea.	Acyclovir with AZT: increased in vitro antiretroviral activity. Acyclovir with alpha interferon: increased in vitro antiretroviral activity. Acyclovir with probenecid: 30% decreased acyclovir clearance. *Note: At this printing, the safety of acyclovir during pregnancy has not been firmly established. If you require acyclovir during pregnancy, report it to the mfg's registry (800/722-9292, ext. 58465).*
Mx: Repeat pap smear every 3 months after treatment. Px: Condoms.	Cryosurgery: Involves freezing of the cervix, causing a watery discharge for approximately 2 weeks post therapy. Podophyllin: scarring, nausea, vomiting, fever, confusion, rarely coma, renal failure. Laser therapy: local pain, vaginal discharge, periurethral swelling, vulvar itching, swelling. Other Tx may be recommended, consult your doctor on side effects.	*Podofilox and podophyllin should not be used during pregnancy.* Self-treatment is not recommended. Consult medical provider before initiating any HPV therapy.
Px: Condoms. Topical antibiotics, chemicals, and creams are NOT effective for prevention. Mx: Monitor for increases in syphilis titers which may indicate a treatment failure or relapse. Watch for neurologic manifestations.	Benzathine and procaine penicillin: skin rashes, edema, fever, chills. Amoxicillin: see Chancroid. Ceftriaxone: see Chancroid. Antibiotics often cause yeast infection. See candidiasis prophylaxis.	Penicillin with tetracycline: may antagonize bactericidal effect of penicillin. Amoxicillin with penicillin: hypersensitivity.
Px: Acidophilus bacteria (e.g. lactobacillus) in capsule form or 8 oz. of yogurt daily. Garlic capsules also found useful. A study is underway considering fluconazole as Px in women with low CD4 counts. Note: Many antibiotics used to treat HIV-related infections are "broad-spectrum" meaning they kill all bacteria in your body including the useful flora naturally found in the vagina which helps to prevent overgrowth of candidiasis. If taking antibiotics, take acidophilus as well.	Oral azoles: liver toxicity Creams and suppositories are often oil-based and may weaken latex condoms and diaphragms. Refer to product labeling for further instructions.	Avoid alcohol with azoles. Fluconazole: avoid warfarin, rifampin, oral contraceptives. Clotrimazole: raises liver function tests. Ketaconazole: antacids and ddI may interfere with absorption, so take them 2 hrs. apart, avoid tuna fish. *Only topical azole therapies are recommended for use during pregnancy, most effective: clotrimazole, miconazole, butoconazole, and terconazole. A 7-day regimen is advised.*

BID = 2 times a day **X** = times **mg** = milligrams **kg** = kilograms (1kg = 2.2 lbs)

GENERAL HEALTH GUIDELINES

At any T-cell level

- ❒ Reduce stress.
- ❒ Reduce alcohol/drug use.
- ❒ Good diet - fresh food, "safe' eating.
- ❒ Quit smoking.
- ❒ Only have safer sex.
- ❒ Get sufficient rest.
- ❒ Pneumovax.
- ❒ Yearly flu shot.
- ❒ Yearly testing for tuberculosis.
- ❒ Baseline testing and as indicated testing for syphilis, toxoplasmosis, cryptococcus and hepatitis B.
- ❒ Regular dental check-ups with cleaning, use Listerine or Peridex twice a day after brushing.
- ❒ Regular eye exams, especially if past problems or T-cell count is below 300.

Extra Guidelines For Women

- ♀ PAP smear every six months.
- ♀ If HPV or other abnormality present, follow up and more frequent testing.
- ♀ Self breast exam monthly, clinical exam yearly, baseline mammography if age 35 or older.

DOIN' IT FOR THEMSELVES 5

How women can deal with physicians

Vivian had to see a new dermatologist for an HIV-related skin problem. The doctor entered the room with a couple of residents, looked at her chart, and said, "Sex or drugs?" "Excuse me?" Vivian said. "Sex or drugs?" he repeated. "I don't do drugs anymore," she said. "And sex with you? I don't think so."

While Vivian's answer is unusual, her experience isn't. Many women with HIV report that the first question asked by a doctor is how they were infected. This sets up a judgmental tone for a visit.

Women's relationships with physicians can be colored by inequalities based on gender, race, and class. What can you do to minimize these differences and gain a mutually respectful, interactive relationship?

Ask questions

Vivian, Lisa, Rosemarie, Jane, and Karen are HIV-positive women from various racial and ethnic groups. But they've all found successful ways to improve communication with their doctors.

Vivian asks physicians their names. "If it's a new face, I ask them how long they've been working with PWAs. This was hard at first. I wasn't aggressive and I wasn't educated. In the Hispanic community, first you pray, and then you give yourself over to the doctor—who is next to God. I don't do that any more."

She asks questions about her treatments as well. "I read about whatever I've got, find out about the side effects of drugs, and I won't let anybody stick something in my arm without knowing what it is," she says.

Vivian suggests keeping a pad of paper with you and making notes about what your doctor says. Then you can ask follow-up questions later or call a hotline or treatment group to find out more. Lisa's physician would leave the room before all her questions were answered. She overcame that. "I put my chair in front of the door, sat down, and said, 'I still have a few questions'."

Make choices

With a mother who was a nurse, Rosemarie always had access to caring physicians. But when she found out she was HIV-positive, her relationships with doctors soured. "Is it because I'm an African-American woman whose life they don't value?" she wonders.

The lesson for Rosemarie and all women is don't accept devaluing behavior from physicians. Ask why you're being treated poorly, find out to whom you can report the behavior, or find a new doctor.

Rosemarie found another reason to find a new physician. "I had a terrible case of ano-genital herpes," she said. "The doctor kept giving me a drug even though it didn't do anything. Finally I went to a specialist used by a lot of gay men who suggested a different treatment. It worked."

Jane made a choice to travel two hours in order to see a physician she trusts. "We have a cooperative relationship. I go in with my little list. I read everything, monitor my health, and keep a record of how I'm feeling."

The gyn visit

A key part of a woman's healthcare program involves gynecological and pelvic exams. But a pelvic exam can be at best unpleasant or embarrassing and at worst humiliating and degrading. That experience can affect a woman's relationship with other physicians.

Women with HIV should get gyn care every six months—preferably from a health care worker who specializes in HIV.

When getting gyn care, sit up until the provider comes into the room. When you're lying down, you're in a vulnerable position, so tell your providers that you want to know what they're going to do before they do it.

Gynecologists may not see women as at risk for HIV. For three years, Karen experienced chronic vaginal yeast infections and other symptoms now recognized as HIV-related. She only got tested when she found out an ex-lover had died of AIDS. None of the many doctors she visited ever asked her, a white woman, any questions about her sexual history related to HIV risk.

To have a good relationship with any healthcare provider, you must take an active part in your own healthcare.

Read treatment newsletters, talk to treatment groups, and talk to other women about their experiences. Write down your symptoms, write down your questions, and take the lists with you. And if you have to, learn to be "uppity" and demand respect.—

HIV POSITIVE WOMEN AND THEIR CARE 6

Most people in this country have been conditioned to think of HIV infection as affecting only certain groups. Women make up one of the groups that too few people have thought of as being susceptible to HIV infection. In fact, physicians often discount the possibility of a woman having HIV.

In addition, the living circumstances of many HIV positive women present a competing set of priorities. The majority of these women are relatively young and in their child-bearing years. They are often married or in some significant relationship, and many of them have children. Their HIV status may have to take second, third, or fourth place behind whatever else is going on in their lives. And society reinforces this notion, teaching women that once they become mothers or wives other interests must come first.

Your First Time

At initial evaluation, an HIV-positive woman would undergo all the same tests that a man would to figure out where she stands in the course of her HIV progression. CD4 counts and viral load are measured, but neither one of these is a completely accurate indicator of disease progression. The physician should also perform other baseline serologic tests to find any other active infections in the blood that might present a problem. Tuberculosis, hepatitis, cytomegalovirus, and toxoplasma are just a few, and they are not unique to women.

The big distinction between men and women in terms of baseline evaluation lies in the genital tract. All women, regardless of HIV serostatus, need to have a gynecological evaluation. If you are HIV-positive, certain gynecological or genital tract conditions may be harder to treat or may have a more accelerated course. The best example of this would be human papilloma virus (HPV) infection. There are good data showing that women who have dual HIV & HPV infection are more likely to have dysplasia (inflammation of the cervix) or signs of more advanced HPV infection. So any woman appearing for initial HIV evaluation needs to have a pelvic exam, a PAP smear, and an assessment for other conditions or the presence of other sexually transmitted diseases (STDs), such as Chlamydia or gonorrhea. A Pap smear will determine any signs of cervical dysplasia, something a woman is not otherwise going to know that she has. It is characterized by changes on the surface of the cervix that a physician will only notice through histologic examination of the cervical cells.

After the initial visit, the woman needs to have regular gynecological evaluations. Women who have CD4 counts greater than 500 should have a baseline pelvic exam and Pap smear (a test for cancer of the genital tract that will show whether skin cells have undergone pathological changes). If the Pap smear is normal, another should be taken after six months. If it remains normal, then she should get a Pap smear done at least yearly while the CD4 count remains greater than 500. Once the CD4 count falls below 500, the Pap smear should be done every six months (*editors note: some recommend that all HIV+ women have Paps every six months).* And women who are sexually active not only need to have Pap smears done, but also an evaluation for other STDs that they might have acquired between exams.

Complications and Treatments

The major female-specific conditions would all be related to gynecological conditions, and more advanced cases of cervical dysplasia are commonly seen in HIV-positive women. In terms of therapy, no one knows whether a different approach should be taken for HIV-positive than for HIV-negative women. The regular kinds of therapy for cervical dysplasia, from cone biopsies to cauterization to drug treatments like acutane, are all being tested in HIV-positive women to see what the best response may be. There is some suggestion that HIV-positive women are more likely to have recurrences of cervical dysplasia and to have less complete responses to various therapies.

Vaginal Candidiasis

Vaginal candidiasis is an infection of the genital tract caused by candida, a yeast. Symptoms are typically a white, cheesy discharge, and the woman may experience discomfort or itching. It is treated with either topical therapy (creams and lotions), troches (which are antifungal "lozenges" inserted intravaginally), or systemic treatments such as ketoconazole or fluconazole in pill form. The form of therapy depends on how often the woman is having episodes of vaginal candidiasis and what her response to the particular therapy may be. Some woman have two or three episodes a year, respond to local therapy, and don't need to take any drugs between infections. Others have repeated episodes and need to take chronic suppressive therapy in the form of a pill, for example. The lower the CD4 count, the more likely you are to have more bouts, but this varies depending on the individual.

Human Papilloma Virus

HPV infection is transmitted through genital sexual contact. Infection with this virus is commonly seen in HIV-negative women, but the frequency of HPV infection increases in HIV-positive women. The immunosuppression of HIV appears to make it easier for HPV to express itself. It is not uncommon for HIV-positive women to be infected with several different types or strains of HPV, some of which are closely associated with cervical cancer or more advanced stages of dysplasia. HPV infection can also cause a range of conditions: genital warts (easily identifiable during a pelvic exam) or cervical dysplasia, identified by examination of the cervix or Pap smear. A Pap smear, therefore, is critical to determine if you have cervical dysplasia secondary to HPV infection.

HPV infection is not the only cause of cervical disease, but advanced cases of cervical dysplasia are more closely associated with HPV infection. Any kind of genital tract infection, including all STDs, can cause mild cervical disease or inflammation. So if a woman has an abnormal Pap smear, it needs to be followed up to see whether she has another kind of genital tract infection causing an inflammation of the cervix. Some of the changes in cervical inflammation specifically point to HPV infection. But any infection of the genital tract and the cervix can cause inflammation. In most cases, if you treat the STD, the inflammation will go away. Certain types of HPV infection, although STDs, are more likely to progress to cervical cancer if left untreated.

Cervical Cancer

Cancer of the cervix is the result of advanced dysplasia that has gone untreated. No randomized trials have been conducted to determine which therapeutic approach (radiation therapy versus radical surgery), is better than another for the treatment of cervical cancer. And no distinctions have been made for HIV-positive women versus HIV-negative women. However, the severity of the cancer as well as the underlying HIV infection is important. HIV-positive women who have severe cervical cancer are more likely to be in the advanced stages of their underlying HIV infection. Most likely, they have lower CD4 counts and may not be able to recover from radical surgery. But a woman who is asymptomatic and active might recover nicely.

Menstrual Problems

HIV-infected women often experience problems with menstruation; they develop irregular cycles, or they stop menstruating - that is, become amenorrheic. Probably disturbed regulation of hormone production is the cause, but we know next to nothing about this. We also know next to nothing about a woman's hormonal balance and the effects that drugs may have on her hormone production. It is the case that female athletes who have less than a certain amount of body fat can become amenorrheic. And clearly HIV-associated wasting is seen in HIV-positive women and may be related in some way.

A Long Way to Go

No one really knows the right approach to many of these conditions. The general STDs such as trichomoniasis (an itchy inflammation of the vagina caused by a parasite), Chlamydia, syphilis, and gonorrhea, for instance, have not been thoroughly studied in the realm of HIV. There is anecdotal evidence, however that the response to standard therapies may be less than satisfactory for HIV-positive women. No randomized trial has been conducted either to support or to refute this, but two large-scale national studies, HERS and WIHS, are following the course of HIV-positive women and HIV-negative women who are at risk. Most of these study groups are completely enrolled, but sometimes they are continuing to enroll. Any woman who is particularly interested in finding out about these issues or helping researchers obtain answers to them might think about participating in one of these trials. Calling (800) TRIALS-A will refer you to a trial coordinator in your area.

The take-home message for women, then, is to have regular Pap smears, pelvic exams, and an assessment for other kinds of infections. If the Pap smear is abnormal, you need to be followed up to determine what the cause is. Then your physician can make recommendations about whether to treat the infection with normal antibiotics or HPV-directed interventions. Women who are HIV-positive need to find a physician who is interested not only in the disease and the conditions that women may develop, but also in the issues surrounding women's needs. And support from medical professionals—in the form of on-site child care, coordinating visits for the mother and child at the same time, and helping the mother set up a system at home in which she has time to take her own medications and care for herself—will go a long way to helping women succeed in their medical care.

HIV Progression and Survival in Women

Do HIV infected men and women progress to AIDS at different rates?

Most recent evidence suggests:

- ♀ Women do not progress faster than men
- ♀ Women's survival is not shorter than men's after controlling for socioeconomic factors and differing CD4 counts at time of diagnosis

For women to prevent progressing more quickly to AIDS several things are important:

- ✓ Early diagnosis
- ✓ Consistent medical care
- ✓ Access to, and use of, antivirals
- ✓ Prophylactic medicines (i.e. Bactrim for PCP)
- ✓ Aggressive treatment for opportunistic infections (OIs)

Earlier studies suggested that women did progress faster to AIDS and that survival was shorter after diagnosis. Why?

- Many early studies included few women
- Decreased access to health care among women

Besides Gynecology, Should Women Receive Different Treatment Than Men?

In general, recommendations for treatment, including prophylactic therapy (preventive treatment) are the same for women as for men. Most studies showing benefits of medicines including antivirals (AZT, ddI, etc) have been done on HIV+ men, so there is much we do not know. There is very few data that exist showing different responses to medicines between men and women.

Clinical Complications of HIV in Women

Opportunistic Infections (OIs)

- Women and men equally as likely to get most OIs except KS (Kaposi's sarcoma) KS is more common in gay men.
- T-cell count (CD4 count) is the most important predictor of risks of getting a particular OI
- Herpes simplex virus (HSV) infections and "yeast in the throat" (also called esophageal candidiasis or esophageal thrush) occur more frequently in women with AIDS
- One study linked pattern of yeast infection to T cell count

Vaginal Yeast Infections:
at any T cell count

Oral Thrush:
(also called oral candida) may be 1st indicator of HIV. Be aware of soreness on tongue, inside of mouth, white spots on tongue or inside mouth. Thrush can occur when T cell count is less than 500 or from taking antibiotics at any T cell count

Esophageal Candidiasis:
(Thrush in throat) Usually occurs only when T cell count is less than 100

Non-opportunistic Infections:

Bacterial Pneumonia:
Seen more frequently in HIV positive women who use IV drugs than in gay men

Urinary Tract Infections:
("Bladder infections", UTIs)

Skin Diseases and Thrombocytopenia (Low Platelet Counts):
Less common in HIV +women than men

Gynecological Manifestations

The following occur **more frequently and are more severe** in HIV+ women:

Vaginal Candidiasis
Cervical Abnormalities (Abnormal Pap Smears, Dysplasia)
Pelvic Inflammatory Disease (PID)
Herpes Simplex (Genital)
Menstrual Abnormalities

Vaginal Candidiasis:

- ❍ Also known as vaginal yeast infection, candidiasis, fungal infections
- ❍ Symptoms: vaginal itching, discharge that looks like cottage cheese, may or may not have bad odor
- ❍ More common in HIV+ women, harder to get rid of and often comes back
- ❍ Treatment:
  - Topical antifungals such as Clotrimazole (Mycelex), Monistat-7, Terazole; although these become less effective as T cell counts go down
  - HIV+ women may need longer medicines in pill form such as Itraconazole 200 mg twice a day (b.i.d.), Fluconazole 150 mg once a day (q.d.) (Diflucan)
- ❍ Recurrences of vaginal candidiasis may occur frequently
- ❍ As T cells go down, some women may need preventive treatment (prophylaxis) with Fluconazole (Diflucan) or Ketoconazole (Nizoral)
  - Fluconazole (Diflucan) 50 mg three times a week reduced the frequency of vaginal yeast infections in women with T cells less than 500

Pap Smears, Dysplasia, and Cervical Cancer

What is a Pap Smear?

- ◆ Screening test for cervical cancer.
- ◆ Cervix is the neck of the uterus (womb) located in the vagina
- ◆ Part of a pelvic exam
  - Involves gently scraping the cervix with a wooden stick which looks like a tongue blade and by twirling a small brush inside the cervix to pick up more cells.
  - Cells are spread on glass slide and sent to a lab

☞ **Get Pap Smears Every Six Months!**

INTERPRETING THE RESULTS OF PAP SMEARS

We've all had the experience of hearing about some medical results from a health practitioner, but we still didn't know what the results were. It can be very confusing. Below are the guidelines and terminology generally used with regard to pap smears.

If Your Results Indicate:	This Means:
Satisfactory or WNL (Within Normal Limits	Great! Repeat PAP smear in six months.
Inadequate or Insufficient for Interpretation	Slide does not have enough cells or there are no cells from the inside of the cervix. Repeat in 2-3 months
Inflammatory Changes	Conditions which make it impossible to get a good view of the cells: **Vaginal infections** like yeast, trichomonas, bacterial vaginosis; **Cervical infections** like gonorrhea, chlamydia; **Herpes simplex;** **Recent douching or sex:** don't put anything into vagina (tampons, douches, etc.) or have sex for 48 hours before Pap smear; **Hormonal changes** like menopause, Atrophic vaginitis (dry vagina due to low estrogen levels and menopause), treated with estrogen creams) **Treat all infections before repeating Pap Smear!**
Atypia or Squamous Cell Atypia	Cells may be atypical because a woman is on "the pill", or for the above reasons under inflammatory changes, or failure to get pap smear under the best conditions. Recurrent atypias require Colposcopy (looking at the cervix under magnification). If condition is diagnosed and treated, then reschedule the PAP in 6-8 weeks (A more detailed article is later in this section). **If Atypia or CIN 1**, then repeat pap in 2-3 months. **If low CD4 or Pap shows dysplasia**, Colposcopy within 6 weeks.
Dysplasia (CIN-Cervical Intraepithelial Neoplasia)	CIN 1, CIN 2, CIN 3, precancer, SIL. The grade (1,2,3) represents the extent of the problem with 1 being the least extensive.

What If the Pap Smear Results are Abnormal?

Treat any condition that can be treated before going further such as Vaginal thrush, Trichomonas, Bacterial Vaginosis (Gardnerella), or any STDs (Gonorrhea, Chlamydia)

Abnormal Pap Smears, Dysplasia, Cervical Cancer

Colposcopy

A Colposcope is a magnifying instrument used to magnify the surface of the cervix. Does not go inside the vagina.

- Examiner looks for abnormal cells on the cervix, vagina, vulva. Finds abnormal looking areas and takes samples of them (biopsies).
- Return in 2-3 weeks to get results.

Dysplasia (pre-cancer)

This is diagnosed using a Pap Smear, confirmed by colposcopy, and biopsy. In many cases it is caused by HPV, it also occurs in women who were sexually abused as children.

HPV (Human Papilloma Virus)

- Sexually transmitted
- Causes warts. Some you can see; others are invisible.
- Can cause dysplasia if HPV infects the cervix

Dysplasia: Outcome

If dysplasia is found on the cervix one of three things occur

- Regression (self-healing)
- Remains on cervix, unchanged, for many years
- Progresses to cervical cancer, usually over several years
- Dysplasia can also occur on the vagina or the vulva

Cervical cancer can be prevented by Pap Smears EVERY SIX MONTHS and Treatment of Dysplasia

Dysplasia: Treatment

Cryotherapy (cryo or freezing):

Abnormal area of cervix is frozen, falls off and healthy tissue replaces it. Takes 2-3 weeks for healing. Expect a heavy, watery discharge until healed.

Cone Biopsy:

Small wedge of tissue is removed under general anesthesia while you are asleep

Electronic Therapy (LEEP or LOOP):

Abnormal tissue removed with a wire loop and electric current.

Laser Therapy:

Abnormal area of cervix is removed with laser. Benefits are less bleeding and quicker healing.

Natural Remedies:

Called Escharotic Treatment. Herbal packs that cause tissue sloughing are applied to the cervix in the doctor's office twice weekly for several weeks. There are also nutritional supplements, suppositories and herbs.

Cervical Cancer

- Women may not have symptoms
- In advanced stages, symptoms are pain, vaginal discharge, bleeding between periods

Treatment

- If very small— a cone biopsy
- If cancer is not entirely removed by biopsy, more radical measures will have to be considered, such as hysterectomy (in the past chemotherapy has been used with limited success)
- If cancer has spread beyond the cervix, then radiation treatment is warranted

Part 1: What You Need To Know About Pap Smears

In my experience as a nurse, I have found that many women come to the health clinic for a Pap smear, knowing that it is important to their health, but often not really knowing what the test is for. Women often hate to have the test, because many have been treated roughly or with insensitivity in the past. Common complaints that women have include:

- the provider doesn't speak to them before the exam;
- they are asked to "assume the position" before meeting the doctor;
- the speculum is cold and/or it is inserted roughly;
- the provider doesn't make eye-contact, or even makes odd comments or jokes during the examination; and
- little or no information is provided about the procedure, the medical findings or tests.

What is a Pap Smear?

A pap smear is a routine part of a pelvic examination. It involves collecting a sample of cells by gently scraping the cervix with a wooden stick that looks like a tongue depressor, and by twirling a tiny brush inside the cervical canal to pick up more and different types of cells. The cells are spread on a glass slide, prepared, and sent to a laboratory for examination. It usually takes a week or less to get your results, but sometimes can take as long as two weeks.

Regular Paps are important

The Pap test is a very good, safe, non invasive screening test that all women should have at least once a year. HIV positive women, because of increased rates of abnormal Pap smears, should have a Pap test taken every six months.

Preparing for a Pap test

You can help ensure that your Pap test will be accurate by doing the following:

1) Schedule the Pap test to take place about two weeks before your next expected period. If your periods are absent or infrequent, schedule the appointment, but if bleeding starts unexpectedly call to ask what to do;
2) Do not put anything in your vagina (tampons, douches, medications, creams or foams)

What if your Pap is Abnormal?

Let's say you have just received news that your Pap test returned with an abnormality. What is your first thought? In my experience, most women assume it means they have cancer. Women are understandably afraid and worried. How do most women receive the news? Usually there is a letter or a phone call. If the woman is fortunate, her medical provider calls, explains the result, reassures her that it can be treated properly, describes the procedures for follow-up care, and gives thoughtful instructions regarding what to do next. On the other hand, many women get the news from a clerk, a nurse, or a letter. Often the caller does not answer even basic questions about what is involved in follow-up

care. A letter may come with an instruction sheet explaining procedures that need to be done, such as colposcopy, but this is not personal enough to relieve the fear. Of course, in the worst case scenario, the woman is not contacted at all about her result, due to some deficiency in the system that she is counting on to take her health seriously.

What To Do If Your Pap Smear Results Are Abnormal

First, Treat Any Conditions You Can. If a Pap smear shows any degree of abnormality, you can be scheduled for a colposcopy (an exam that looks at the cervix under magnification). However, it is very important for the clinician to treat any condition that can be treated first, before making the referral for a colposcopy. These conditions include:

- Vaginal Thrush
  (also called candida, monilia, or fungal vaginitis);
- Trichomonas, Bacterial Vaginosis
  (also called BV or gardnerella);
- Atrophic Vaginitis (due to low estrogen levels/menopause, and treated with estrogen creams);
- Herpes Simplex Infection; and
- any other condition.

Understanding Your Pap Smear Results

The cytologist (the person who reads your Pap smear) should use the standardized "Bethesda system" to report the results of your Pap smear using one or more of the following terms:

Inadequate or Insufficient for Interpretation

This slide lacks enough cells or fails to show cells from inside the cervical canal. It should be repeated in 2 to 3 months. (A Pap smear should not be repeated in less than six weeks, to increase the likelihood of getting an adequate sample.)

Atypia or Squamous Cell Atypia

These cells show minimal changes, and may be "atypical" due to use of oral contraceptives (the "pill"), presence of a vaginal infection or condition, or a failure to obtain the smear under the best conditions. Any problems that are identified should be corrected, and the smear should be repeated in 2 to 3 months. Recurrent atypias require colposcopy (looking at the cervix under magnification). Some clinicians will schedule a colposcopy for all HIV positive clients with atypia.

CIN—Cervical Intraepithelial Neoplasia (Dysplasia)

These reports are graded as CIN I, CIN 2 or CIN 3. This is the condition that is also called dysplasia (meaning "abnormal development"), "pre-cancer" or Squamous Intraepithelial Lesion (SIL). The grade (1, 2 or 3) represents the extent of the problem.

- "CIN 1" means that one-third of the sample has dysplasia or pre-cancer;
- "CIN 2" two-thirds of the sample has dysplasia;
- "CIN 3" entire sample shows cells with dysplasia.

Carcinoma-In-Situ (CIS)

On a Pap smear, this report means the same thing as a CIN 3. In other words, the entire sample shows abnormal cells.

Other Conditions

The Pap smear may report additional conditions that may affect the accuracy of the smear.

"Inflammatory changes" refers to many findings that can interfere with a good view of the cells. Vaginal infections such as yeast, trichomonas, bacterial vaginitis, and other germs may be noted as present on the slide. Inflammation can be due to hormonal changes (such as in menopause), use of birth control pills or other medications, or recent douching or intercourse.

As stated earlier, all conditions identified on the smear must be corrected or treated before obtaining another smear.

Then, Schedule Another Pap Smear Or A Colposcopy

If a condition is diagnosed and treated, it is quite reasonable to reschedule the Pap test in 6 to 8 weeks. This is because any of these conditions can give an inaccurate Pap result, either falsely positive or falsely negative. If the Pap returns with Atypia or CIN 1, some clinicians will repeat it in 2 to 3 months before making a referral. However, if you have a low CD4 (T-cell) count, or signs of immune compromise, it is probably best to go right to colposcopy. This is because not enough is really known about how cervical disease progresses in women with low CD4 cells. Also any Pap that shows moderate or severe dysplasia (CIN 2, CIN 3, or CIS) should be evaluated by colposcopy within 6 weeks. The appointment should not be scheduled when you are menstruating.

The Colposcope is a magnifying instrument (which looks something like a microscope) with a lens that can be focused on the vulva, vagina and cervix. It rests on a stand, and the examiner looks through it. The colposcope does not go inside the vagina. It magnifies the surface of the cervix.

In general, the examiner is looking for abnormalities in cells on the outside of the cervix, in the vagina, and even on the vulva. There can also be abnormalities of the inner lining of the cervical canal (columnar cells). Like with the Pap smear, the degree of abnormality is graded, and in general, the same terms are used. The difference is that with a colposcopy, abnormalities are evaluated using a tiny sample of cervical tissue. This process is called a biopsy.

The purpose of using the colposcope is to find the most abnormal-looking areas, and to take samples of them (biopsies). Biopsies hurt, like a sharp pinch, followed by cramping. After having a biopsy, a woman may have some spotting or bleeding for a day or two, and must not put anything into the vagina during the 2 to 3 days it takes for the biopsy to heal.

Colposcopies and biopsies are intended for diagnosis only, not for treatment with the exception of a treatment called a cone biopsy. Therefore, you must be scheduled to return to the clinic or doctor in 2 to 3 weeks for treatment and consultation, depending on how long it takes to get the biopsy report back. When you return, the diagnosis should be shared with you. If the biopsies agree with the Pap, and do not indicate invasive cancer, a local treatment of the cervix is planned.

Part 2: What You Need To Know About Cervical Dysplasia

Dysplasia is a medical term that means "abnormal development." Cervical dysplasia is the abnormal development of cells that grow on the cervix. Cervical dysplasia (also called "pre-cancer") is diagnosed using a Pap smear, confirmed by colposcopy and biopsy (see Part I).

An important factor that can lead to abnormal cell growth is the presence of a virus, called human papillomavirus (HPV). HPV is a virus that can cause warty growths on the skin, the feet or the genitals. Warts look like firm, raised, white or grayish, cauliflower looking bumps that form separately or in clusters. There are over 20 sub-types of HPV; some cause warts you can see and some are invisible.

When HPV infects the cervix, it can cause dysplasia. Thus, dysplasia is actually a condition of abnormal growths on the cervix.

HPV infection that leads to genital warts or cervical dysplasia is sexually transmitted. In fact, most sexually active people have been exposed to HPV. However, most HPV infections cause no symptoms in men or women.

Research indicates that dysplasia in women is also associated with smoking, vitamin deficiencies, poor nutrition, and sexual intercourse at an early age. Women with HIV seem to be more likely to have dysplasia than other women.

When dysplasia is found on the cervix, one of three things may occur. The woman's immune response may heal the affected area and the dysplasia may "regress." The dysplasia may also remain on the cervix, unchanged, for many years. Unfortunately, the third possibility is that the area with the dysplasia may change into cervical cancer. This change is called "progression," and usually happens over a period of several years.

Because many HIV positive women have dysplasia, extra care must be taken to look for and prevent cervical cancer in these women. In rare cases, dysplasia can also occur in the vagina and on the vulva, so these areas need to be inspected carefully during the pelvic exam.

How Is Dysplasia Treated?

Once a woman has been diagnosed with cervical dysplasia, the following treatments are adequate for treating it.

Cryotherapy ('Freezing")

This is most commonly used because it is an easy technique to learn, it can be done in an office without anesthesia, and the equipment is inexpensive. The "cryo unit" holds a gas tank attached to a probe that can touch the cervix. The gas gets very cold under pressure in the tank, and the cold probe is held against the abnormal areas until the tissue is frozen. The frozen tissue dies, sloughs off, and if all goes well, new and healthy tissue replaces the "bad" tissue. The healing process takes 2 to 3 weeks, and the woman usually has heavy, watery discharge during this time. She should not put anything into the vagina during healing.

Cone Biopsy

In a cone biopsy, a wedge of tissue (about the size of the end of your thumb) is removed. This procedure is done if the dysplasia is severe, if it may extend up into the cervical canal, or if the Pap report and biopsies do not agree on the degree of abnormality. A cone biopsy can be done by surgery under general anesthesia, by LEEP under local anesthesia (see below) or by laser under general anesthesia (see below).

Electronic Therapy (also called LEEP or Loop)

In this therapy, a thin wire loop and electrical current are used to remove and destroy abnormal tissue. The diagnostic procedure may remove the entire area of abnormal tissue, eliminating the need for further treatments. However the woman still should schedule follow-up care and to learn the results of her biopsy.

Laser Therapy

Laser therapy uses intense light to destroy abnormal tissue

Natural Therapies

Naturopaths are doctors who use "natural," herbal and traditional remedies, instead of traditional medicines and treatments. There is literature which describes naturopathic remedies for dysplasia. In all cases, the literature advises proper diagnosis by colposcopy, close follow-up, and referral for more conventional therapy if the problem does not improve or gets worse. The scientific study of these treatments is extremely limited. The treatments include local therapy called Escharotic Treatment, in which herbal packs that cause tissue sloughing are applied to the cervix in the doctor's office twice weekly for several weeks. The woman is also instructed about nutritional supplements, dietary changes, suppositories and herbs.

Part 3: What You Need To Know About Cervical Cancer

What Is Cervical Cancer?

When a Pap smear detects dysplasia, a further examination is done with a Colposcope, and a biopsy of the abnormal tissue is taken. If the biopsy report confirms invasive cancer, a process called "staging" must be performed. Staging is a series of tests and evaluations that will determine where the invasion has spread, and whether or not the organs are involved. When the Centers for Disease Control and Prevention (CDC) added cervical cancer to the list of AIDS-defining illnesses in 1993, they specified that the cancer must be invasive, and it must extend beyond the cervix itself. Some AIDS activists and women's advocates feel that this requirement is too stringent; we hope to treat any dysplasia or micro invasive cancer before it spreads beyond the cervix.

Cervical cancer is a cancer of the cervix. The cervix is part of the uterus that opens during childbirth. You can feel it with your fingers inside of the vagina. A sexually transmitted virus called human papillomavirus (HPV) is known to be one of the causes of cervical cancer. HPV doesn't always cause cancer. About one-third of all sexually active women have been exposed to HPV, yet very few have cervical cancer. HPV may also be responsible for cancer in the vagina, vulva, anal-rectal area (in men or women), and on the penis. We also know that factors such as smoking and cervical trauma from childhood sexual abuse have a causal effect in cervical cancer.

Cancer starts out in a few cells, but gradually grows in size, usually over a period of years. The earliest stage of cell abnormality is called dysplasia. When dysplasia is treated, cancer can be prevented. (See Part 2.) When the growth can be seen and felt during a pelvic exam, it is called a tumor. If it is not treated, it grows and invades nearby areas, such as the vagina. Eventually cancer cells will travel to distant places in the body such as the lymph nodes, rectum or bladder. If cervical cancer is not treated it is life-threatening.

Treating Cervical Cancer

A very small cancer ("micro invasive" cancer) may be able to be totally removed by a procedure called a cone biopsy. In this type of biopsy, a larger piece of the cervix is removed. This can be done in a doctor's office, or in the hospital. If a cone biopsy is performed, the tissue is examined very carefully to see if all of the cancer cells have been removed.

If the cancer cannot be entirely removed by the cone biopsy, the woman may need to consider more aggressive treatments, combinations of treatments or repeated surgical interventions. If the cancer continues to spread, the woman may have to consider having a hysterectomy (removal of the uterus) to prevent the further spread of the cancer. Sometimes the lymph nodes in the pelvic area are also removed, and this is called a radical hysterectomy. If the cancer has already spread beyond the cervix, the treatment will usually be radiation and sometimes chemotherapy.

Can Cervical Cancer Be Prevented?

Absolutely! Cervical cancer can be prevented by regular screening and proper treatment of dysplasia. This is a powerful reason for women to get annual Pap smears and gynecological check-ups, HIV-positive women should have an exam and Pap every six months. But be sure to see a provider who knows about HIV!

MENSTRUAL DISORDERS 9

Anecdotal reports indicate that menstrual disorders are more common in HIV+ women although the reason is yet unknown. There clearly needs to be greater research conducted in this area. Presently, we can conclude the following:

- ❒ There is no association between T cell counts and the frequency of menstrual abnormalities
- ❒ Abnormal bleeding makes it difficult to predict when a woman is pregnant and difficult to protect sexual partners from exposure to blood.
- ❒ When HIV+ and HIV- injecting drug users were studied, HIV+ women had more amenorrhea (no periods) and more bleeding between periods than HIV- women

HIV AND PREGNANCY 10

Does Pregnancy Lead to Faster Progression of HIV?

Available data are contradictory, but most of the evidence suggests that pregnancy does not lead to faster progression of HIV. Previous studies have shown that T cell counts go down throughout pregnancy and then normalize 3-4 months after delivery.

Vertical Transmission (Passing HIV from mother to baby)

- ❒ 25%-30% of children born to HIV infected mothers not taking AZT will be HIV+
- ❒ Transmission decreased to 8.3% in mothers taking AZT during pregnancy (ACTG 076)

ACTG -076: Women with T cell counts over 200 took AZT(500 mg/day) during weeks 14-34 of pregnancy, then received IV AZT during labor and delivery (AZT by vein). Newborn was given AZT syrup for six weeks.

- ❒ 10-15% of vertical transmission is associated with breastfeeding

Intrapartum Transmission

Intrapartum transmission refers to passing HIV from mother to baby while baby is in the womb or at delivery.

- ❒ Substantial proportion of HIV transmission occurs at delivery or during the third trimester (last three months)

Predictors of Risk of Transmission

- ❒ Viral load (women with higher viral load have more risk of transmission to baby)
- ❒ Route of delivery (vaginal vs cesarean section) C-section is slightly lower
- ❒ Birth order (of twins) first born twin is at higher risk of infection

Postpartum Transmission (passing HIV from mother to baby after baby is born)

- ❒ 10-15% of vertical transmission is associated with breastfeeding which is not recommended for mothers with HIV

Importance of Viral Load

What is Viral Load?

Viral load test measures the amount of virus present in the blood. RNA is the genetic material of HIV. HIV viral load test measures the amount of HIV specific RNA. One viral load test (PCR) results are reported as copies of HIV RNA per ml of plasma (blood).

- ❒ Recent study of 30 HIV+ women giving birth, 20 of 22 mothers that did not transmit HIV to their babies had low viral load (less than 30,000 copies per milliliter of blood.)
- ❒ 8 of 8 transmitting mothers had high viral loads.
- ❒ AZT reduced-transmission of HIV by two thirds in ACTG 076 by reducing viral load.
- ❒ AZT appears to have minimal side effects for the babies' transient anemia (iron poor blood) which was later reversed.
- ❒ Nevirapine is being studied in late pregnancy to decrease viral load.
- ❒ Clinical trials of protease inhibitors and other reverse transcriptase inhibitors (drugs like AZT, ddI, ddC, d4T, 3TC) are being planned.

TREATMENT DURING PREGNANCY

Pregnant women with HIV often aren't given enough (or any) information about how their pregnancy affects their treatment standard of care. Again, there is far too much we don't know, but the following are some guidelines.

- ❒ HIV+ women who are pregnant with T cell counts under 200 should receive PCP prophylaxis.
  - The preferred PCP prophylaxis is Bactrim (Septra), one pill a day to prevent Pneumocystis Carinii pneumonia (PCP) the most common OI in PWAs with less than 200 T-cells
  - Dapsone is used in PWAs who are allergic to Bactrim. Less is known about the risk in pregnant women.
  - Aerosolized Pentamidine is reasonably safe but less effective than Bactrim

Treatment of Other Opportunistic Infections During Pregnancy

Herpes Simplex Virus (HSV)

- ❒ Acyclovir (Zovirax) cuts down on herpes outbreaks but it has not been demonstrated to be safe in pregnancy.
- ❒ Women who have a herpes outbreak near the time of delivery should deliver by C-section so baby won't come into contact with herpes lesions in the birth canal.

Tuberculosis

- ❒ Women should be screened for exposure to TB with a TB skin test (called a "PPD") as part of the initial prenatal workup.
- ❒ Active TB disease requires treatment with 4 drugs.
- ❒ TB prophylaxis (prevention in women who have come into contact with someone with TB but who don't have active TB themselves) with Isoniazid (INH) may be started during the second trimester

Toxoplasmosis

Toxoplasmosis is an infection caused by a parasite found in raw meat, dirt, and the stool of cats.

- ❒ HIV+ women (and men) should not change cat litter, should cook all meat thoroughly and wash hands well after gardening.
- ❒ Toxo is a problem for both HIV+ and HIV- pregnant women.
- ❒ Crosses the placenta during pregnancy and can result in miscarriage, stillbirth, or in the baby being born with Toxo (Congenital Toxo)
- ❒ Toxo should be treated in pregnancy with the usual doses of pyrimethamine combined with sulfadiazine or clindamycin

The Bottom Line In Pregnancy:
Get Prenatal Care from an Obstetrician Well Versed in HIV Care.

PREGNANCY PRESENTS SPECIAL CONSIDERATIONS FOR WOMEN WITH HIV [11]

Decisions about pregnancy can be complex and difficult for any women. If you are HIV+ and considering a pregnancy, you must think about added factors:

- ❒ HIV can be transmitted from HIV+ mother to infant, although there is recent good news (see preceding information)
- ❒ Caring for your child may be interrupted by HIV-related illness at some point
- ❒ Pregnancy may affect your health and immune system
- ❒ If you have syphilis, you will need special care. Babies born to women with untreated syphilis can become seriously ill or die.

Much is still not known about HIV and pregnancy, and HIV+ pregnant women have to make many decisions in the face of uncertainty. No one should try to force you into any decision about the continuation or termination of a pregnancy. We encourage you to take advice and counsel, up to the point that you feel comfortable, from friends, family, support groups and others who care about you. But do not hesitate to tell people who offer advice that while you appreciate their concern, the decision of whether to continue or terminate your pregnancy is yours.

If you are considering pregnancy, it is also important that you have someone who is knowledgeable and unbiased to help you come to your decision. Your health care provider may be able to help you with this. Other resources include WISE - Women's Information Service and Exchange, (404) 817-3441; the Feminist Women's Health Center, (404) 874-7551, the AIDS Hotline For Women (404) 888-9991, AIDS Survival Project women peer counselors and AIDS Survival Project Treatment Resource Library at (404) 874-7926.

PELVIC INFLAMMATORY DISEASE 12

Pelvic Inflammatory Disease (PID) comprises a spectrum of inflammatory disorders of the upper genital tract in women. PID includes endometriosis, salpingitis, tubo–ovarian abscess and pelvic peritonitis. Clinically, some health care providers report that PID occurs more frequently in HIV positive women than in women who are HIV negative and lead to more complications that are more likely to require hospitalizations.

Diagnosis

A confirmed diagnosis of salpingitis and a more accurate bacteriologic diagnosis is made with laparoscopy (an incision is made near the navel through which a very small tube is inserted to take a look-see). Since laparoscopy is not always available or feasible, the diagnosis of PID is often based on clinical findings and culture or antigen detection tests of specimens of the lower genital tract.

Treatment

Treatment of PID in HIV positive women depends on the cause of the PID and the women's T cell counts. Parenteral antibiotics may be appropriate in some cases. Other women may require only ceftriaxone 250 mg IM injection followed by a 14–day course of doxycycline 100 mg po bid. If patient should be hospitalized but cannot be, add metronidazole 1.0 gm po bid. Reexamination is important 2–4 days after initiating treatment, with close follow–up after that.

HERPES SIMPLEX VIRUS (HSV)

Genital herpes is a chronic viral disease for which no known cure exists. Genital herpes has been associated with an increased risk of getting, and transmitting HIV. Many women may have no symptoms of herpes until her immune system is suppressed enough for the virus to take hold and cause symptoms.

Diagnosis

Genital herpes presents as small, painful little blisters, usually in clusters. The blisters usually break open before they dry and heal. During an outbreak, the lymph nodes are typically tender and perhaps swollen. HSV should be considered in the differential diagnosis of any painful, ulcerative genital lesion. Diagnosis is confirmed by herpes culture of the lesion.

Intervention

In HIV positive women, recurrences may be more frequent, more severe and last longer than the typical 7 to 10 day course. Repeated acyclovir (Zovirax) treatment or higher doses of acyclovir may be necessary to control symptoms. Symptoms often recur when medication is discontinued.

Acyclovir treatment provides partial control of the signs and symptoms of herpes episodes, reduces viral shedding and the duration of disease if women are treated within 6 days of the onset. It does not affect the subsequent risk, frequency or severity of recurrences, unless the woman takes it as prophylaxis. Renal (kidney) function must be monitored closely and dosing interval extended for renal insufficiency.

During the acute phase initiate therapy with acyclovir 200 mg po 5 times/day x 10 days. If HSV is non–responsive, increase acyclovir to 400 mg po bid–qid.

In women with frequent recurrences (more than 6 recurrences annually), suppressive therapy of acyclovir 200 mg po qid or 400 mg po bid or if necessary 400 mg po qid indefinitely is recommended. Safety and efficacy have been documented among persons receiving daily therapy for up to three years.

Acyclovir resistance has been noted in HIV positive women on chronic acyclovir. If acyclovir resistance is confirmed by HSV culture and sensitivity testing, infectious disease consultation should be sought.

CHANCROID

Chancroid is a STD identified as a major risk factor for sexual transmission of HIV. Genital ulceration is thought to act as an entry point for the virus. Women may be unaware of the presence of ulcers.

Diagnosis

Chancroid is characterized clinically by acute, painful ulcers on the external genitalia accompanied by tenderness and swollen lymph glands. Women with cervical chancroid tend to have multiple ulcers. Cervical and extragenital ulcers (on places other than the genitals) occur in about 10 percent of women. Diagnosis is based on a culture for Haemophilis ducreyi.

Intervention

Chancroid is treated with ceftriaxone 250 mg IM (single dose) or erythromycin 500 mg po qid x 7 days or ciprofloxacin 500 mg po bid x 3 days. Treatment failure is more common in HIV positive women, especially with single dose treatment. As the susceptibility of H. ducreyi varies by geography, response should be monitored clinically and by susceptibility patterns.

SYPHILIS

Since 1980, the incidence of primary and secondary syphilis has increased by more than 200 percent. This occurs at a time when ulcerative STDs are known to make it easier to transmit HIV. All sexually active women with syphilis and their partners should be encouraged to be counseled and tested for HIV.

Syphilis is a sexually transmitted disease (STD). It often occurs with HIV infection but can be hard to recognize and treat in persons who have HIV. Untreated syphilis can cause severe nerve, heart, and blood vessel damage and even death.

It is important to tell your doctor about your full sexual and medical history. Some questions you may want to ask include:

- What are the tests for syphilis?
- How often should I be tested?
- How is syphilis treated?
- Will I need tests to make sure the treatment worked?
- How can I avoid passing syphilis to others?

Your doctor may give you blood tests to learn if you have syphilis and to see how far it has progressed. You also may need other tests. You should be tested for syphilis anytime you think you have been exposed to an STD.

If you have syphilis, you should tell your sex partners or persons with whom you have shared needles. Your health care provider or a health department worker can help you do this and tell you whether the law in your state requires that your sex partners be notified.

Penicillin shots are the usual treatment for early syphilis. For more advanced disease, you may require intravenous (IV) penicillin and perhaps a hospital stay. If you are allergic to penicillin, you may need to see a specialist.

Diagnosis

Primary syphilis: Chancre (lesion) not exquisitely tender. Dual infection of syphilis and HSV not uncommon. The main test for syphilis, called an RPR, does not become positive until 3–6 weeks after initial infection. An early negative test does not exclude syphilis. If negative, repeat at 6 weeks. There are other tests that become positive at 3–4 weeks.

Secondary syphilis: It is usually associated with generalized lymphadenopathy (swollen, tender lymph glands). Women often have fevers and may show signs of hepatitis and/or nephritis (kidney dysfunction).

Latent syphilis (early: less than 1 year's duration; late: more than 1 year's duration, indeterminate neurosyphilis) the CDC recommends a lumbar puncture (spinal tap) on all HIV positive women with the following test results: serum FTA/ABS antibody titer > 1:32; neurologic symptoms; women who cannot be prescribed penicillin for treatment.

Treatment

Primary, secondary, early latent (< 1 year): benzathine penicillin G 2.4 million units IM (some sources recommend weekly x 3 weeks).

Late (> 1 year): benzathine penicillin G 2.4 million units IM weekly x 3 weeks OR penicillin G 2 to 4 million units IV q 4 hrs x 10 days, or penicillin G procaine 2.4 million units IM qd plus probenecid 500 mg po qid, both for 10 days; and either one followed by benzathine penicillin G 2.4 million units IM weekly x 3 weeks.

Serial RPRs should be drawn at 1, 2, 3, 6, 9, 12 months and every 6 months thereafter. Whenever possible, penicillin allergic patients should be referred to an infectious disease specialist for desensitization because reports show that tetracycline and erythromycin may be inadequate for HIV positive women.

RESOURCES SPECIFIC TO WOMEN WITH HIV

LOCAL:

Sisterlove, Inc
1432 Donnelly Avenue, SW
Atlanta, GA 30310
(404) 753-7733
Services primarily for HIV+ women of color including housing, day programs, and support groups.

Women's Information Service and Exchange (WISE)
125 5th Street, NE
Atlanta, GA 30308
(404) 817-3441
Monthly newsletter; treatment information, resource center, advocacy; and support groups.

REGIONAL:

Life Force: Women Fighting AIDS
165 Camden Plaza East, #310
Brooklyn, NY 11202
(718) 797-0937
Support groups, safer sex parties, referrals, outreach, health fairs.

New Jersey Women & AIDS Network (NJWAN)
5 Elm Row #112
New Brunswick, NJ 08901
(908) 846-4462
Education and advocacy.

Cascade AIDS Project Women's Phone Network
620 SW 5th Street, Suite 300
Portland, OR 97204
(503) 223-5907
Testing and counseling, prevention/outreach, advocacy, client services, support groups and HIV education programs.

NATIONAL:

National Women and HIV/AIDS Project (NWAP)
807 Massachusetts Avenue
Washington, D.C. 20002
(202) 547-1155
Advocacy training, public policy, and program models for women living with HIV and AIDS.

National Women's Health Network
1325 G Street, NW, Lower Level
Washington, DC 20005
(202) 347-1140
Advocacy around health care issues and legislature, health education.

WORLD (Women Organized to Respond to Life-threatening Diseases)
P.O. Box 11535
Oakland, CA 94611
(510) 658-6930
Monthly newsletter

Women Alive
4410 Sepulveda Blvd.
Culver City, CA 90230
(213) 965-1564
Quarterly newsletter, WomensCare Center (health care) in Los Angeles.

For referrals for doctors or clinics experienced in treating women with HIV contact:

AIDS Survival Project
828 W. Peachtree Street
Atlanta, GA 30308
(404) 874-7926
or
(WISE) Women's Information Service and Exchange
125 5th Street, NE
Atlanta, GA 30308
(404) 817-3441

FOOTNOTES

1 Project Inform Fact Sheet
10/11/94

2 Project Inform Fact Sheet
10/11/94

3 Project Inform Fact Sheet
10/11/94

4 Project Inform Fact Sheet
10/11/94

5 by Marion Banzhaf
Positively Aware, Fall 1993

6 by Christine Chandler, RN
Being Alive, December 1991

7 by Kathleen Squires, MD.
Positively Aware, Jan/Feb, 1996

8 Excerpted from a presentation given by Edith Biggers, MD., Board of Directors, AIDS Survival Project. Physician at Fulton County Health Department Ryan White Clinic.
February 1996

9 by Risa Denenberg, FNP
WISE Words, December 1995
Women's Information Service and Exchange
125 5th Street, NE, Atlanta, GA 30308
(404) 817-3441

10 Excerpted from a presentation given by Edith Biggers, MD.
February 1996

11 Excerpted from a presentation given by Edith Biggers, MD.
February 1996

12 by Erin McBreen
Positively Aware, Spring 1994

13 Seattle-King County Dept of Public Health
AIDS Prevention Project
(206) 296-4999
February 1991

Updated and revised by Christopher D. L. Miller, R.N., May 1995 and
Alicia A. Culver, June 1996

GLOSSARY

GLOSSARY

Abscess: A circumscribed collection of pus appearing in acute or chronic localized infection, and associated with tissue destruction and, frequently, swelling.

ABT-538: See Ritonavir

Accelerated Approval: Government approval of a new treatment for sale based on early surrogate marker data from clinical studies. The purpose of accelerated approval is to speed the availability of new drugs for life-threatening HIV-related conditions.

Access: The degree of ease with which the consumer can secure health services. Along with availability, access is a key criterion used to measure the adequacy of a health care system.

Acemannan (Carrisyn): The potentially active ingredient in aloe vera juice. A few studies have suggested that acemannan has direct activity against HIV and also up-regulates cell mediated immunity.

Acid-Fast Bacillus (AFB): Any bacillus that is resistant to decolorization with acidified organic solvents after staining with a dye. Used as the basis of a test for identifying Mycobacterium tuberculosis and other mycobacteria.

Acidophilus: Bacteria found in yogurt that help restore a supportive bacterial environment to an intestinal tract affected by disease and antibiotics. Ingesting acidophilus may also be useful in preventing candidiasis (thrush), and in the vagina (yeast infection).

Acquired Immunodeficiency Syndrome (AIDS): A manifestation of infection with the human immunodeficiency virus (HIV) characterized by the presence of one or more diseases as defined by the Centers for Disease Control and Prevention (CDC). These diseases occur following a depression of an individual's immune system function. The affected person becomes susceptible to unusual infections and malignancies (see "opportunistic infection").

ACTG: ACTG stands for AIDS clinical trial groups (also called ACTU, with "units" instead of "groups"). ACTGs are a network of medical centers throughout the country that conduct federally funded clinical trials of drugs for treating people with HIV infection. ACTGs are sponsored by the National Institute of Allergy and Infectious Diseases (NIAID). Taken together, the ACTGs are the largest trials of drugs for treating HIV infection in the world: they have the largest budgets, the largest number of investigators, and the largest number of participants.

Acupuncture: An ancient treatment which relieves pain and symptoms by inserting thin needles, beneath the surface of the skin.

Acute: Refers to intense, short-term symptoms or illnesses that either resolve or evolve.

Adherence: The act of following a prescribed therapeutic regimen.

Adrenal Glands: A pair of endocrine organs (located above the kidney) that produce hormones, including steroids and adrenaline.

Adverse Event: A toxic reaction to a medical therapy.

Advocacy: Action taken on behalf of individuals by themselves, their families, health care providers, activists, or others to ensure appropriate access to and availability of services and fight discrimination.

Aerosolized Pentamidine: A drug used for Pneumocystis Carinii pneumonia (PCP) prophylaxis that is dispersed through a nebulizer in a mist. When inhaled, it goes directly to the lungs.

AFB Isolation: A specific type of hospital isolation for persons with acute M. tuberculosis. Its purpose is to prevent the spread of infection during the infectious phase of the disease.

AIDS Related Complex (ARC): A term, no longer in use, referring to symptoms seen in persons infected with HIV who have not been diagnosed with AIDS. ARC is now often called "symptomatic HIV disease." ARC includes persistent symptoms such as: fatigue, fever, swollen glands, diarrhea, and unintentional weight loss.

AIDS Defining Illness: One of a list of serious illnesses that occurs in HIV-positive individuals and is reason for an AIDS diagnosis according to the CDC's definition of AIDS. Among these conditions are PCP, MAC, AIDS dementia complex, AIDS wasting syndrome, invasive cervical cancer, Kaposi's sarcoma and CMV retinitis.

AIDS Dementia Complex: AIDS dementia complex is the term used for the dementia that appears to result from HIV's directly infecting the brain. Dementia means the loss of intellectual capacity, including the loss of memory, judgment, or concentration.

Airborne Transmission: Process by which an infectious agent passes through the air to infect susceptible individuals by droplet infection (e.g. sneezing, coughing).

Alkaline Phosphatase: An enzyme produced in the liver as well as in bone and other tissues. Elevated serum levels of the enzyme are indicative of liver disease, bile duct obstruction in particular.

Allergic Reactions: An extreme sensitivity to things such as drugs. Some allergic reactions can be life threatening.

Alpha Interferon: 1 of 3 major classes of interferon that the body produces in response to viral infections. In people who are HIV positive, elevated levels of "acid labile" alpha interferon may indicate disease progression. Genetically engineered alpha interferon is an FDA-approved treatment for Kaposi's sarcoma (KS), anogenital warts and chronic hepatitis B.

ALT (alanine aminotransaminase): An enzyme produced by the liver that plays a role in protein metabolism, like AST. Abnormal elevations of ALT often accompany liver disease like hepatitis. ALT is also called SGPT (serum glutamic pyruvic transaminase).

Alternative Therapies: Treatments that are not based in traditional Western medical practice. Also referred to as complementary medicine.

Amino Acid: Any of twenty nitrogen-containing acids that are the building blocks for proteins and

required for human growth. They are the basic structural unit of proteins, the unique sequences of which are specified by genes.

Amoebiasis: Infection of the intestines, liver or other organs with amoebae. Amoebae are contracted through contact with fecal material through food or rimming. Symptoms may include diarrhea, cramping, jaundice, anorexia and weight loss.

Americans with Disabilities Act: (Public Law 101-336) Passed in July 1990. This legislation establishes equal opportunity for persons with disabilities regarding employment, public accommodation, transportation, state and local government services, and telecommunications.

Amitriptyline: Amitriptyline hydrochloride (or, e.g., Elavil) is one of a group of drugs called tricyclic antidepressants that are grouped together because of their chemical similarities. Tricycle antidepressants are used to treat depression and the peripheral neuropathy that causes painful feet. In many cases, the dose is arbitrary: many people start on a low dose and have the dose increased as necessary. Side effects are common, but usually not severe enough to stop treatment. The main side effects are drowsiness, weakness, and fatigue; dry mouth; constipation; and low blood pressure and dizziness. These side effects are all dose-related, meaning the higher the dose, the more severe the side effect. Because the drugs cause drowsiness, they are often given before bedtime.

Amphotericin B: The antibiotic amphotericin B is the standard treatment for many infections caused by fungi, including most of the fungi that affect people with HIV infection: Candida, Cryptococcus, Histoplasma, Coccidioides, and Aspergillus. Amphotericin B, which is given only by vein, is highly effective. Unfortunately, it is also one of the most toxic antibiotics known. The most important side effects include kidney damage, anemia , disturbances in the balance of electrolytes, nausea and vomiting, fever and chills, and phlebitis or inflammation of the vein into which the drug is injected. Many of these side effects can be reduced in severity or eliminated by stopping the drug, by continuing the drug at a lower dose, or by giving other medications at the same time that will counteract the side effects. Because of amphotericin B's toxicity, other drugs, like ketoconazole and fluconazole, are given when they are considered to be as effective or nearly as effective.

Amylase: Amylase is a starch-splitting enzyme secreted by salivary glands and the pancreas to aid digestion of food. An increase in amylase serum levels may indicate pancreatitis, a possible life-threatening consequence of ddI.

Anabolic: Refers to cellular synthesis of organic molecules.

Anabolic Steroid: A synthetic steroid used to increase muscle mass and weight. Anabolic steroids are versions of the natural hormone testosterone but have fewer masculinizing effects. Anabolic steroids have been used to reverse AIDS-related wasting syndrome on an individual basis, but trial data are lacking.

Analgesic: An agent or drug that relieves pain.

Androgen: A masculinizing hormone such as testosterone.

Anemia: Anemia means that the number of red cells in the blood is reduced. Red blood cells are responsible for delivering oxygen to all parts of the body. When the reduction is severe, the result is

fatigue. Anemia can be caused by HIV infection itself, by an opportunistic infection, or by several of the drugs commonly taken by people with HIV. Drugs often responsible include trimethoprim-sulfamethoxazole, other sulfa drugs, pentamidine, amphotericin B, and AZT. When the anemia is severe, it can be corrected with transfusions. When drugs are responsible, the drugs can be reduced in dose or discontinued.

Anergy: State of being unable to react immunologically to an antigenic stimulus. Usually used to denote lack of response to specific antigens injected into the skin of the forearm (i.e. a TB test).

Angiogenesis: The process of new blood vessel growth. Tumors and Kaposi's sarcoma lesions stimulate angiogenesis to supply themselves with blood.

Anorexia: The lack or loss of appetite for food.

Antibiotics: Antibiotics are drugs made from natural substances (as opposed to drugs made artificially) that inhibit the growth of microbes. Antibiotics may be effective against any of the classes of microbes including bacteria, fungi, parasites, and viruses that cause infections.

Antibody: Antibodies are proteins and are the part of the complex immune system that attacks any substance protein or microbe that is foreign to the body. Certain cells called B lymphocytes recognize these substances as foreign and manufacture antibodies that inactivate or eliminate the foreign substance. The foreign substance that the antibodies attack is called an antigen . For most antigens, the B lymphocytes take one or two weeks to produce antibodies; for HIV, however, the time required may be 6 months or more.

Antifolate: An agent that inhibits the effects of folinic acid.

Antigen: Any foreign substance that causes an immune response when introduced into the body.

Antigen Presenting Cell (APC): A cell, such as a macrophage or dendritic cell, that digests foreign bodies and exhibits the resulting pieces of the protein (antigen) on its surface in an effort to find and activate the CD4 T-helper cell responsive to that antigen.

Antiretroviral Drug: A drug that reduces the replication rate of HIV. The most commonly used are zidovudine (AZT), dideoxyinosine (ddI), ddC and D4T.

Antioxidant: A substance that inhibits oxidation or reactions promoted by oxygen or peroxides.

Antisense: A complement piece of DNA or RNA that recognizes another piece of DNA or RNA by base-pairing. Antisense drugs are designed to block viral genetic instructions, marking them for destruction by cellular enzymes, in order to prevent the building of new virus or the infection of new cells.

Antiviral: A substance or process which destroys a virus or suppresses its ability to reproduce.

Aphasia: Nerve disorder which causes speech difficulty or loss.

Aphthous Ulcers: Single or multiple recurrent, well-circumscribed painful ulcers that develop on nonkeratinized oral mucosa.

Aspergillus: A fungus that infects the lungs, causing a disease as aspergillosis. The infection can spread through the blood to other organs and cause lesions of the skin, ear, nasal sinuses or lungs, as wells as occasionally the bones, mèninges, heart, kidneys, or spleen.

AST (Aspartate Aminotransaminase): A liver enzyme that plays a role in protein metabolism, like ALT. Elevated serum levels are a sign of liver damage from disease or drugs. AST is also known as SGOT (serum glutamic oxaloacetic transaminase).

Asthenia: Weakness, debility.

Asymptomatic: Asymptomatic means the absence of symptoms. The asymptomatic person feels healthy.

Ataxia: Lack of muscular coordination.

Atovaquone (Mepron): A medication for mild to moderate cases of PCP as well as for salvage treatment of toxoplasmosis. A new, more absorbable liquid formulation has entered the market. Atovaquone should be used with caution along with rifampin and fluconazole since these drugs can lower atovaquone blood levels.

Atrophy: A wasting or shrinking of cells, tissue, organs or muscle.

Auto Immune: When the body attacks its own defense system.

Azidothymidine (AZT): Also known as zidovudine and Retrovir a nucleoside analog which interferes with reverses transcriptase, an enzyme HIV needs to convert RNA to DNA to reproduce and continue to infect other cells. This is an FDA approved drug. Resistance may develop over time. Side effects may include granulocytopenia, anemia, fatigue, headaches, muscle pain, nausea and rashes.

Azithromycin (Zithromax): An antibiotic approved for the treatment of chlamydia and bacterial infections of the skin and respiratory tract. It may also have activity against MAC, toxoplasmosis and cryptosporidiosis. Possible side effects include nausea, dizziness, sensitivity to sunlight and vaginal candidiasis.

Bacille Calmette-Guerin (BCG): A vaccine containing a bovine derived, live, attenuated strain of mycobacterium that has been used in countries other than the United States as immunization against tuberculosis.

Baclofen: Baclofen is a drug used to control muscle spasms. The most common side effect is drowsiness and, in large doses, severe sedation, lack of coordination, and lowered functioning of the heart and lungs.

Bacteremia: The presence of bacteria in the blood.

Bacterium: A microscopic organism composed of a single cell.

Bactrim: A drug used for PCP prophylaxis. see TMP/SMX.

Barbiturates: Barbiturates are drugs commonly used to treat insomnia, anxiety, and seizures. Examples of barbiturates are amobarbital (or Amytal), pentobarbital (or Nembutal), phenobarbital, and secobarbital. All barbiturates affect the central nervous system: low doses cause mild sedation, and high doses can lead to deep coma. When barbiturates are used for sedation, they remain effective for only about two weeks. As a result, alternative drugs are generally preferred to treat insomnia. Prolonged use of the drug can cause physical dependence, psychological dependence, and tolerance (it takes more of the drug to do the same thing). Discontinuing barbiturates can cause difficult withdrawal symptoms.

Baseline: A known value with which later measurements can be compared (e.g., baseline T helper cell count, baseline hemoglobin level). This is usually the first test you get.

B-Cell (B-Lymphocyte): A type of lymphocyte that is a precursor to plasma cells. During infections, individual B-cell clones multiply and are transformed into plasma cells, which produce large amounts of antibodies against a particular antigen on a foreign microbe. This transformation occurs through interaction with the appropriate CD4 T-helper cells. See B Lymphocytes.

***b*DNA (branched DNA):** A test for measuring the amount of HIV (as well as other viruses) in blood plasma. The test uses a signal amplification technique, which creates a luminescent signal whose brightness depends on the viral RNA present. Test results are calibrated in numbers of virus particles per milliliter of plasma. *b*DNA is similar in results, but not technique, to the PCR test.

B Lymphocytes: B lymphocytes are the white blood cells, called lymphocytes. They are responsible for producing antibodies. B lymphocytes are different than T lymphocytes (including CD4 cells, also called T4 cells), which are also part of the immune system, but which work against a different group of microbes using different mechanisms. See B-cell.

Benzodiazepines: Benzodiazepines are a class of drugs commonly used to treat anxiety, insomnia, seizures, and painful muscles. Examples of benzodiazepines include alprazolam (or Xanax), diazepam, flurazepam hydrochloride (or Dalmane), lorazepam (or Ativan), midazolam maleate, oxazepam (or Serax), prazepam (or Centrax), temazepam (or Restoril), and triazolam (or Halcion). In general, all benzodiazepines act in similar ways and seem to be equally effective. Most physicians prefer benzodiazepines for treating anxiety and tension. Compared to barbiturates and meprobamate, and when given at the doses that relieve anxiety, they are less addictive and produce less sedation. People taking benzodiazepines should be aware that the drug may impair their ability to perform activities that require mental alertness and physical coordination. Benzodiazepines can also cause physical dependence and symptoms of severe withdrawal if the drug is stopped suddenly after being used regularly for a long time.

Beta-2 Microglobulin: An immune system protein found in the blood. Elevated blood levels of this protein are associated with immune activation, replication of HIV and weakly predictive of worsening of the disease associated with HIV infection.

Beta Carotene: A form of carotene, precursor to vitamin A. Beta carotene may have beneficial effects on the immune system.

Bilirubin: A red pigment occurring in the liver bile, blood and urine. Bilirubin is the product of the

breakdown of hemoglobin in red blood cells. It is removed from the blood and processed by the liver, which secrets it into the digestive tract via the bile. An elevated level in blood serum is an indication of liver disease or drug-induced liver impairment.

Bioavailability: The extent to which an oral medication is absorbed in the digestive tract and reaches the bloodstream.

Biopsy: A procedure to get a piece of tissue for examination under a microscope. The microscopic changes in tissue often provide a diagnosis, and stains and cultures often reveal the infecting organism.

Bitter Melon (MAP-30): The fruit of a Chinese vine related to the cucumber. Bitter melon has been used as a treatment for diabetes, gastrointestinal complaints, some cancers and viral infections. It most recently has been tried as a treatment against HIV (administered most often by enema). Little information about efficacy or proper use is available.

Blastogenic: A process that occurs in response to infection by agents such as bacteria and viruses, in which lymphocytes mature and prepare to divide and reproduce.

Bleach: Chlorine bleach is highly effective in killing HIV within minutes. It is available at most grocery stores and is commonly recommended for killing any virus or other microbe that may be in such body fluids as blood, saliva, and stool. Bleach is usually diluted 1:10, or one part of bleach in ten parts of water (except when used for cleaning syringes, then it should be used full strength). This dilution can be applied to surfaces or in the washing machine for clothes.

Blood count: Blood is composed of red blood cells (erythrocytes) which carry oxygen to all parts of the body, white blood cells (leukocytes) which help make up the immune system, and platelets (or thrombocytes) which are required for blood clotting. All three kinds of cells can be counted under a microscope. A low red blood cell count is called anemia (see above); a low white blood cell count is called leukopenia , and a low platelet count is called thrombocytopenia . People with HIV infection commonly have low red counts, low white counts, and low platelet counts. A blood count is a routine procedure for clinical laboratories; it is a relatively simple, inexpensive, and standard test to evaluate people with HIV infection.

Blood Brain Barrier: A protection for the brain which prevents organisms from getting into or damaging the brain and nervous system. This may also be an obstacle for drug therapies.

Body Fluids: The various liquids found in the human body. Of these fluids, only blood, semen, vaginal secretions, and breast milk have been found to contain concentrations of HIV that are high enough to infect another person. Saliva, sweat, tears, and urine have not been shown to transmit HIV.

Bone Marrow: Bone marrow is the tissue in the central portion of many bones where blood is manufactured. Bone marrow can be withdrawn (by placing a needle in the hip bone) and analyzed to detect abnormalities in the production of red blood cells, white blood cells, or platelets.

Bone Marrow Suppression: A side effect of many anticancer and antiviral drugs, including AZT. Bone marrow suppression leads to a decrease in white blood cells and platelets. Such reductions in turn result in anemia, bacterial infections and spontaneous or excess bleeding.

Bowenoid Papulosis: A papillomavirus associated disease involving changes in tissue in the anogenital region.

Bronchi/Bronchioles: The tubes or airways of the lungs that lead from the trachea or windpipe to the alveoli.

Bronchitis: A disease marked by inflammation of the bronchial tubes in the lungs.

Bronchoscopy: A curved and flexible tube is used to look into the lungs and may be used to suck samples of tissues for examination. Usually performed with some anesthesia.

Buffered: Refers to pills coated with a special substance that neutralizes stomach acid. Drugs are buffered to reduce stomach upset or increase absorption by the intestines.

Burkitt's Lymphoma: An AIDS defining opportunistic infection which is a cancerous growth or tumor usually in the jaw or stomach which may be cause by Epstein-Barr Virus (EBV). It is diagnosed by X ray, CAT scan, MRI and/or biopsy.

Buyers' Clubs: Buyers' clubs are groups, or even individuals, that make underground drugs (drugs not approved by the Food and Drug Administration and thus not available as licensed drugs in the United States) available to people with HIV infection. The advantage of a buyers' club is that it offers the person with HIV infection the opportunity to take drugs that might require long periods of testing before becoming widely available. The disadvantage is that the drugs are untested and could be toxic or useless. The Buyer's club we have in Atlanta is AIDS Treatment Initiatives at (404) 874-4845.

Cachexia: A general weight loss and wasting occurring in the course of a chronic disease.

Cancer: Uncontrolled cell growth or malignant cells which may expand and destroy normal surrounding tissue resulting in tumors.

Candida: Refers to Candida albicans, a yeast-like fungus that can infect the skin, nails, blood or mucous membranes throughout the body, including the esophagus (swallowing tube), vagina, intestines and lungs. Oral candidiasis is referred to as thrush. Oral and vaginal candidiasis are often early signs of an impaired immune system in HIV positive individuals. Oral candidiasis may be white or red.

Candidiasis: An infection with a fungus of the Candida family generally C. albicans, that most commonly involves the skin, (dermatocandidiasis), oral mucosa (thrush), respiratory tract (bronchocandidiasis) and vagina (vaginitis). Candidiasis of the esophagus, trachea, bronchi or lungs is an indicator disease for AIDS.

Carbohydrate: An organic molecule made up solely of carbon, hydrogen and oxygen. Carbohydrates made be made up of only one or two components (mono- or disaccharides, also called "sugars") or be complex chains of repeating units (polysaccharides or "starches," also the cellulose in plant cell walls).

Carcinogen: Any substance which can cause or encourage the growth of cancer.

Carcinoma: a malignant tumor that may spread throughout the body.

Carcinoma In Situ: An early, curable stage of cancer in which the tumor has not spread beyond a defined site.

Cardiomyopathy: Myocardiopathy; a disease of the myocardium, or heart muscle. Most cardiomyopathies are thought to be due to viruses or toxins.

Cardiovascular: referring to the system that involves the heart and blood vessels.

Catheter: A hollow and usually flexible tube which is inserted into the body to allow fluids to enter or exit the body .

Case Management: System under which the patient's health care and social services are coordinated by one or more individuals familiar with both the patient's needs and community resources.

Casual Contact: In the context of AIDS, refers to non-intimate behaviors such as working, eating, playing, studying, hugging, or holding hands. These activities do not transmit HIV.

CD4 Cells: The blood contains several kinds of white cells, each of which plays a specific role in the immune system. CD4 cells (other names are T4 cells and T-helper cells) are the cells that HIV selectively infects. The number of CD4 cells is frequently used to indicate the stage of HIV infection. Healthy people without HIV infection usually have around 1,000 CD4 cells in every milliliter of blood; counts of 400 to 700 are considered abnormally low, but not alarming. People with AIDS usually have counts of less than 200. Counts of less than 200 do not indicate AIDS, but suggest severe weakening of the immune system. The CD4 count is a relatively expensive test, but it is an important way of monitoring the state of the immune system. In any one person, however, the count varies considerably: the same laboratory performing the test on the same specimen can show counts that vary by as much as 20 percent. The CD4 count is also influenced by a variety of other medical conditions independent of HIV infection. As a result, although the CD4 count is frequently used to assess progressive disease, changes in the count are sometimes difficult to interpret.

CD4+ Cell Count: The actual number of T helper cells (Lymphocytes) in a cubic millimeter of blood. The CD4+ cell count is significantly lower in people whose immune systems have been affected by HIV. Also known as absolute CD4+ cell count. See CD4 cell or T4 cell.

CD8 Cell: One type of T-lymphocyte which bears the CD8 molecular marker on its surface. Some CD8 cells recognize and kill cancerous cells and those infected by intracellular pathogens (some bacteria, viruses and mycoplasma). These cells are called cytotoxic T-lymphocytes.

CD4/CD8 Ratio: The ration of CD4 to CD8 cells. A common measure of immune system status that is around two in healthy individuals.

Cell: The smallest unit of a living structure.

Cell-Mediated Immunity: Type of specific immune response mediated by cytotoxic T and natural killer (NK) cells.

Centers for Disease Control and Prevention (CDC): The Centers for Disease Control is a federally funded institution located in Atlanta, Georgia. It has three responsibilities: to serve as an epidemiologic and public health resource for state and local health departments; to investigate epidemics; and to keep track of contagious diseases and other diseases important to public health. At present, the CDC is the storehouse for all reported cases of

AIDS in the United States. It provides guidelines for disease prevention and gives advice on safety for health care providers. It is responsible for funding state and local agencies that test for HIV, counsel, and collect data.

Central Nervous System (CNS): The brain, spinal cord, and its coverings (meninges).

Cerebrospinal Fluid: Fluid that bathes the brain and spinal cord. A sample of this fluid is often removed from the body for diagnosis purposes by a lumbar puncture (spinal tap).

Cervical Cancer: An AIDS defining opportunistic infection in women with HIV. It is a cancerous growth or tumor on the uterine wall. It is diagnosed primarily by the Pap smear, there also is a new blood test, not yet widely available, to help detect the presence of cervical cancer.

Cervical Dysplasia: An abnormality in the size, shape, or organization of the cells lining the cervix that can be detected on a Pap smear. If undetected, cervical dysplasia may progress to a more severe lesion; thus, any abnormal finding should prompt further examination.

Cervical Intraepithelial Lesion (CIN): A condition revealed by Pap smear that necessitates further evaluation.

Cervix: The lower, cylindrical terminus (end) of the uterus that juts into the vagina and contains a narrow canal connecting the upper and lower parts of a woman's reproductive tract.

Chancroid: A highly contagious sexually transmitted disease caused by the Hemophilus ducreyi bacterium. It appears as a pimple, chancre, sore or ulcer on the skin of the genitals. The lesion appears after an incubation period of three to five days and may facilitate the transmission of HIV.

Chancre: A primary sore or lesion that forms at the site of entry (or exit) of a disease-causing microorganism, as in syphilis.

Chemoprophylaxis: The use of chemical agents for disease prevention.

Chemotherapy: The use of chemical agents in the treatment of a disease.

Chicken Pox: (See Herpes Zoster)

Childbearing Age: The period of a woman's life during which she is capable of conceiving a child, typically from ages 15 to 44. Many times, this is used to exclude women from participating in clinical drug trials.

Chloral Hydrate: Chloral hydrate is a sedative used to treat insomnia. It is usually taken fifteen to thirteen minutes before bedtime. Using chloral hydrate regularly for more than two weeks often reduces its effectiveness. Major side effects include stomach irritation, residual sedation, or a hangover. Chloral hydrate should be used with great caution in people who are depressed, who may commit suicide, or who have a history of drug abuse.

Chlamydia: The most common sexually transmitted bacterium (Chlamydia trachomatis), that infects the reproductive system. The infection is frequently asymptomatic, but if left untreated, can cause sterility in women.

Chronic: Referring to a process, such as a disease process, that occurs slowly and persists over a long period of time; opposite of acute.

Ciprofloxacin (Cipro): An oral antibiotic approved for the treatment of many common bacterial infections. Sometimes administered to treat MAC in combination with other drugs. Possible side effects include gastrointestinal upset, seizures and rash.

Cidofovir (HPMPC): A nucleotide analog under evaluation for treatment for CMV retinitis and genital warts. Side effects include kidney damage.

Clarithromycin (Biaxin, Klacid): An antibiotic approved for the treatment of MAC and also used for preventing this disease in people with AIDS. Side effects include diarrhea, nausea and abnormal taste. Clarithromycin may cause severe abdominal pain at high doses.

Clindamycin (Cleocin): An antibiotic that may be an alternative treatment for toxoplasmosis and PCP. The most common side effect is diarrhea. Overgrowth of an intestinal bacterium called Clostridium difficile is responsible for the diarrhea during clindamycin therapy.

Client Oriented: Describes medical and social services that are directed toward the client's or patient's needs and interests.

Clinical: Refers to physical signs symptoms directly observable in the human body.

Clinical Trials: Scientifically governed investigations of medications in volunteer subjects. Their purpose is to seek information regarding the products' safety (Phase I) and efficacy (how well it works) (Phase II/III).

Clofazimine (Lamprene): An antileprosy agent sometimes administered in combination with other drugs to treat MAC. Possible side effects include gastrointestinal upset, skin discoloration and rashes.

Clostridium Difficile: People who take antibiotics often develop diarrhea as a side effect. A relatively common and particularly severe cause of this diarrhea is a microbe called Clostridium difficile. Almost any antibiotic can cause this complication, but the most frequent causes are ampicillin, amoxicillin, clindamycin, and a group of drugs called cephalosporins that includes cefixime (or Suprex), cefuroxime, cephalexin (or Keflex), and cefaclor (or Ceclor). People who have diarrhea while taking these or any other antibiotics should stop taking the antibiotics and call their physicians. A test of stool will determine if Clostridium difficile is the cause. If it is, it can be treated with metronidazole or vancomycin hydrochloride. Vancomycin is preferred for serious cases of diarrhea, but it costs about $200 to $300. Metronidazole is less expensive $10 to $20 and equally effective unless the person has severe colitis.

Clotrimazole (Lotrimin, Mycelex): An antifungal drug used primarily during HIV infection as a topical agent for oral and vaginal candidiasis.

CMV (Cytomegalovirus): CMV, which is short for cytomegalovirus, is a herpes virus commonly found in people without HIV infection. Usually the immune system holds CMV in check, and it remains dormant in the body without causing any serious disease. With a severely weakened immune system, however, CMV may cause serious infection. The site of the infection can be in the

eye, lung, liver, gastrointestinal tract, bone marrow, brain, or widespread in many of these areas. The virus can be detected by cultures of blood, cultures of urine, or biopsies of any of the organs that are affected. CMV is difficult to treat: some antibiotics seem to inhibit its growth in the test tube, but no one agrees about when these drugs should be used.

CMV Polyradiculopathy: CMV infection of the peripheral nerves and the spinal roots leading to generalized weakness and paralysis.

CMV Retinitis: CMV infection of the retina of the eye. The lesions it causes lead to deterioration in vision and ultimately blindness if untreated. Requires treatment with a drug which slows the progression of the infection and which must be taken indefinitely.

Coccidiomycosis: An AIDS defining opportunistic infection caused by the fungus Coccidioidcs immitus. The spores of this soil fungus are inhaled and grow in the lungs and may spread through the blood to other parts of the body. The early symptoms are similar to the flu, but may progress to symptoms similar to PCP and lesions on the skin or other organs. It is diagnosed by an microscopic examination of sputum bronchoscopy and/or culture. Because it is mostly limited to the Southwestern United States, it is often called valley or desert fever.

Coenzyme Q: A substance that aids in the oxidation of food within cells to create energy. It is also highly efficient at protecting internal and external call membranes against oxidation and is sometimes proposed as a complementary therapy to combat AIDS-related conditions.

Co-factor: A co-factor is anything microbes, proteins, hormones, genes which makes a disease progress more rapidly. With HIV infection, co-factors are only suspected but may include other viruses (like cytomegalovirus), age, genetic resistance or predisposition, and certain hormone-like substances, called cytokines, released by lymphocytes.

Cognitive: Relating to the process of knowing, based on awareness and reasoning.

Cohort: A group of individuals sharing a demographic or clinical characteristic.

Colitis: Inflammation of the colon, a condition that causes pain and diarrhea.

Colon: The gastrointestinal tract which starts at the mouth and ends at the rectum includes the esophagus, stomach, small intestine, colon, and rectum. The colon and the small intestine are commonly the sites of infections that cause diarrhea. To diagnose problems in the colon, common procedures are colonoscopy and sigmoidoscopy. These procedures permit visualization and biopsy of the colon by passing a tube through the rectum.

Colposcopy: A procedure in which the surface of the uterine cervix is examined through a flexible fiber optic tube for signs of cervical dysplasia or cancer. Colposcopy is a more accurate alternative to Pap smears, but requires considerable more skill and is much more costly.

Combination Therapy: Alternate or simultaneous administration of two or more therapies.

Community-based Organizations (CBOs): Community-based organizations are organizations and agencies that provide services to people in need. AIDS service organizations (ASOs) are community-

based organizations that serve people with HIV infection, as well as providing education and prevention programs for the whole community. The leaders of community-based organizations are lay people, ordinary people who do not come from the government or from organized medicine.

Community Based: Describes services delivered locally or as close to the client's home as possible.

Community Programs for Clinical Research on AIDS (CPCRA): A program involving 17 centers that conduct clinical trials related to HIV in community-based settings. Sponsored by the National Institute of Allergy and Infectious Diseases.

Compassionate Access: When drugs are made available even though not approved by government agencies.

Compassionate Use: A process for providing experimental drugs to very sick patients who have no treatment options. Often, case by case approval must be obtained from the FDA for "compassionate use" of a drug.

Complementary Medicine: Non-mainstream health care provided in addition or instead of standard medical practice.

Complete Blood Count (CBC): A screening of the most important cellular components of the blood. A CBC includes the total white blood count, the counts of types of white blood cells, the red blood count including hemoglobin, and platelet count.

Compound Q (GLQ223): An extract of a Chinese wild cucumber. It is used in China to induce abortions and treat respiratory viruses. In this country, Compound Q has been tried as an anti-HIV treatment.

Comprehensive Care: Care that includes the full spectrum of health educational, social, and related services.

Computerized Tomography Scan (CAT Scan or CT Scan): CAT scans are a particular kind of x-ray that provide a three-dimensional view of the body (Regular x-rays are two-dimensional). CAT scans can be done of the entire body or of parts of it. The person receiving a CAT scan first receives an injection of what is called contrast material that shows up under x-rays. Some people have allergic reactions to contrast materials and should not receive them again. The person receiving the CAT scan is next put into a chamber with a scanner that circulates around the body, making three-dimensional images in parallel sections of about an inch or less. CAT scans are an excellent method for detecting tumors, infections, or other changes in the anatomy of the brain, chest, abdomen, or other parts of the body. They are also expensive, usually costing around $300 to $800.

Condom: A sheath used to cover the penis (and sex toys) during sexual intercourse to prevent conception and sexually transmitted diseases. Correct use of a rubber (latex) condom during every act of intercourse greatly reduces, but does not eliminate, the risk of infection with HIV. Lamb skin or "natural" condoms do not offer protection because they are too porous.

Condyloma Acuminata: Anogenital warts, caused by infection with the human papilloma virus (HPV); a common, sexually transmitted disease. It is usually noncancerous or benign. Also referred to as genital warts or verruca acuminata.

Confidentiality: The right inherent in the contract between the health care provider and patient that ensures that information on the patient's medical conditions will be released to a third party only after explicit permission is obtained from the patient or guardian.

Congregate Living: Any one of a number of housing, shelter, or confinement environments in which a number of individuals live together.

Conjunctivitis: Inflammation of the conjunctiva of the eye, the thin protective membrane of the interior of the eyelids, and the white part of the eye. Also called "Pink Eye".

Consumer: An individual who uses a product or service. In the health care setting, a more general term for "client" or "patient."

Constitutional Symptoms: Symptoms caused by the impact of an illness on the entire body or constitution are frequently referred to as constitutional symptoms. For people with HIV infection, constitutional symptoms may be a result of HIV infection itself or the result of such opportunistic illnesses as pneumocystis pneumonia, tuberculosis, or widespread CMV infection.

Contagious: A disease that is contagious can be passed from one person to another. A disease that is infectious is caused by a microbe. All diseases that are contagious are also infectious; but some diseases, like toxic shock syndrome, are infectious and not contagious. HIV is both infectious and contagious, but is contagious only with specific types of contact.

Continuous Care: Describes care that is maintained without interruption despite changes in site, caregiver, or method of payment.

Control Arm: The group of participants in a clinical trial who receive standard treatment or a placebo, against which the experimental treatment is compared.

Controlled Trial: A clinical study in which one group of participants receives an experimental drug while another group receives either a placebo or an approved standard therapy. When participants do not know which group they are in, the trial is blinded.

Coordinated Care: Describes care that is planned and implemented so as to form a cohesive therapeutic program.

Cortex: The outer portion of an organ.

Corticosteroids: Also known as steroids, glucocorticosteroids, prednisone, and cortisone; Corticosteroids are drugs used to reduce the immune response. Numerous preparations are available that can be taken intravenously, by mouth, or in an ointment applied to the skin. Using high doses of corticosteroids for a long time can be dangerous: they reduce the immune system's defenses against certain infections. Corticosteroids are sometimes considered especially dangerous for people with HIV infection, whose immune defenses are already weakened. Nevertheless, many of the complications of HIV infection appear to result from an overly abundant but misdirected immune response. As a result, these complications of HIV infection respond well to corticosteroids, though the drug should be taken at the lowest doses for the shortest period.

Cortisol: Also called hydrocortisone. A steroid hormone secreted by the adrenal cortex.

Cotton-wool Spots/Patches: Fluffy-looking white deposits on the retina that represent small areas that have lost their blood supply due to blockage of local vessels.

CPCRA: Community Programs for Clinical Research on AIDS, a branch of the NIH's Division of AIDS that supports clinical trials based on local networks of practicing physicians. These physicians collect data on their patients as they participate in a treatment trial.

Creatinine: The product of the breakdown of creatine, an important molecule involved in energy transfer within muscle cells. The level of creatinine in the blood and urine provides a measure of kidney function.

Cross-Resistant: Development of resistance to one agent (or drug) which also confers resistance to another (often similar) agent.

Cryotherapy: The use of liquid nitrogen to freeze and destroy an abnormal lesion; some times used to create scar formation in order to prevent further spread of a condition (e.g., retinitis)

Cryptococcal Meningitis: A fungal infection of the membranes surrounding the brain.

Cryptococcosis: Cryptococcosis is an infection caused by the fungus Cryptococcus neoformans. This fungus can cause infection in otherwise healthy people. In people with HIV infection, however, it is especially severe, frequently causing meningitis. Common symptoms include headache, fevers, vision problems, and seizures. The diagnosis is usually made by analyzing cerebrospinal fluid obtained with a spinal tap . The disease is treated with amphotericin B given by vein or fluconazole given by mouth; when treatment is stopped, the disease tends to recur so that long-term treatment is generally necessary.

Cryptosporidiosis: Cryptosporidia are parasites that infect the intestine and cause diarrhea. This infection, called cryptosporidiosis, can occur in otherwise healthy persons, but the diarrhea generally does not last long and is not severe. Cryptosporidiosis in people with HIV infection often causes devastating diarrhea that persists for months. People with cryptosporidiosis may lose large amounts of fluid and nutrients and, consequently, become severely malnourished. The diagnosis is usually established by simply examining the stool under a microscope to detect the parasite. There is no universally accepted form of treatment except to replace the lost fluids and nutrients.

Cryptosporidium: A parasite that causes cryptosporidiosis. The parasite is transmitted to humans by direct contact with the feces of an infected animal, by ingestion of contaminated food or water, or by oral-anal sex (rimming). The parasite grows in the intestines and bile ducts, and causes severe, chronic diarrhea. In immunocompromised individuals, cryptosporidiosis may become life-threatening.

Culture: A culture, in medical terms, is a medium in which microbes can grow. HIV is grown in cultures containing lymphocytes. If a sample of a person's blood is put into such a culture, and HIV grows, the person is infected with HIV. Other blood tests for HIV are polymerase chain reaction or the p24 antigen test. The usual blood test for HIV detects antibodies to the virus instead of the virus itself. The antibody test is usually preferred because it is less expensive, better standardized, and more readily available.

Cunnilingus: Oral contact with the vagina; going down on.

Curcumin: An ingredient of the spice turmeric. Laboratory studies have suggested that curcumin inhibits HIV replication by blocking the long terminal repeat region on HIV's genes.

Curetting: Scraping of a cavity with a sharp spoon-shaped instrument.

Cutaneous: Pertaining to skin.

Cyclospora: A parasite that causes severe diarrhea in various animals including humans. Common in people with AIDS.

Cyst: A closed sack of fluid or semisolid material in or under the skin which is lined with tissue.

Cysteine: Sulfur-bearing amino acid that makes up part of the compound glutathione.

Cytokines: Chemical messenger proteins released by certain white blood cells, including macrophages, monocytes or lymphocytes.

Cytolytic: Having a destructive effect on cells, causing them to erupt or burst open.

Cytomegalovirus (CMV): A member of the herpes virus family that can cause fever, fatigue, enlarged lymph glands, aching, and mild sore throat. In persons with AIDS, CMV infections can produce hepatitis, pneumonia, retinitis, and colitis. CMV infection may lead to blindness, chronic diarrhea, or death. See CMV.

Cytomegalovirus (CMV) Retinitis: A disease of the eye caused by the cytomegalovirus. See CMV Retinitis.

Cytotoxic T-lymphocyte (CTL): Also called a CD8 cell. A white blood cell in the immune system that targets and kills cells infected with viruses, bacteria, parasites or other microorganisms.

Cytopenia: A reduction in the number of cells found in a clinical specimen.

Cytovene: See Ganciclovir.

Dantrolene (or Dantrium): Dantrolene is one of several muscle relaxants. The most common side effect is muscle weakness that usually disappears after taking the drug for several days. Other side effects include hepatitis , diarrhea, gastric intolerance, depression, insomnia, and frequent urination.

Dapsone: An antileprosy drug used in the treatment and prophylaxis of PCP and other disease; possible side effects include skin rash, fever, and gastrointestinal upset. Dapsone also causes destruction of red blood cells (hemolysis) and reduced absorption of ddI.

DaunoXome: A chemotherapy used for Kaposi's sarcoma consisting of a preparation of daunorubicin encapsulated in liposomes. DaunoXome's main side effect is neutropenia, which can be managed with G-CSF (Neupogen).

ddC (dideoxycytidine, zalcitabine, HIVID): A nucleoside analog that inhibits infection of new cells by HIV. It is FDA approved for the treatment of HIV when used in combination with AZT in patients with CD4 cell counts below 300 who have gotten sicker despite treatment, and as monotherapy following AZT failure. Possible side effects include nerve damage in the hands and feet (peripheral neuropathy) and sores in the mouth.

ddI (didanosine, Videx): A nucleoside analog that inhibits infection of new cells by HIV. FDA approved for individuals intolerant to or failing on AZT and for people who have taken AZT for sixteen weeks or more. Side effects can include nerve damage in the hands and feet (peripheral neuropathy), damage to the pancreas (pancreatitis) and diarrhea.

Degenerative: Progressive deterioration of tissues or organs of the body, leading to structural or functional impairment.

Delavirdine: see NNRTI.

Dementia: Chronic loss of mental capacity, with organic origins that affects a person's ability to function in a social or occupational setting. AIDS-related dementia may be caused by HIV or other infections.

Demodex: Minute mites that inhabit the skin and are usually found in the sebaceous glands and hair follicles.

Dendritic Cell: An immune cell with long, tentacle like branches called dendrites. Among the dendritic cells are the Langerhans cells of the skin and follicular dendritic cells in the lymph nodes. Dendritic cells function as antigen presenting cells.

Deoxidant: An agent that removes oxygen from a substance.

Depigmentation: A partial or complete loss of coloration.

DNA (Deoxyribonucleic acid): A complex protein that is the carrier of genetic information. HIV can insert itself into a cell's DNA and use cell mechanisms to replicate HIV.

Dermatitis: Inflammation, pain, itching or redness of skin.

Desensitization: Gradually increasing the dose of a medication in order to overcome severe allergic reactions. Desensitization procedures have become popular when administering Bactrim for the first time.

Developmentally Oriented: Describes care that is based on the individual's functional level and chronological age. Functional level includes physical, cognitive, psychosocial, and communicative development.

Dextroamphetamine sulfate (or Dexedrine): Dextroamphetamine sulfate, along with methylphenidate hydrochloride (or Ritalin Hydrochloride), stimulates the brain. It is usually given to people with HIV infection with AIDS dementia complex to counter the symptoms of apathy and social withdrawal. The most common side effects are nervousness and insomnia. Both side effects can usually be controlled by decreasing the dose and by avoiding taking the drug late in the day.

Diagnosis: Confirmation of illness based on an evaluation of a patient's medical history, symptoms, and laboratory tests.

D4T: Also known as Stavudine. A nucleoside analog which reverses transcriptase, an enzyme HIV needs to convert RNA to DNA to reproduce and infect other cells. This is not an FDA approved drug. It is not known if resistance may develop over time.

Direct Fluorescent Antibody Staining for Treponema Pallidum (DFA-TP): A specific test (direct fluorescent antibody staining on a biopsy sample) for T pallidum, the organism that causes syphilis. The presence of T pallidum organisms in lesions of early acquired or congenital syphilis in this test is the definitive means of making a diagnosis of syphilis.

Directly Observed Therapy (DOT): A patient takes a medication while under direct observation by another individual. Usually used in antituberculosis treatment.

Distal: Farthest from the center of the body or from a central reference point.

Dose-Escalation: A preliminary clinical trial in which the amount of drug is either periodically increased or increased with each new trial arm that is added. Used to determine how a drug is tolerated in people.

Dose-Ranging: See Dose-Escalation.

Double Blind: A trial design in which neither the subjects nor the participating research investigators are aware of which patients are receiving test drugs and which are receiving placebo or other therapy Believed to promote faster and more objective results, since it eliminates the possibility of bias concerning the test drug's efficacy.

DOX-SL (Doxil): A chemotherapy for Kaposi's sarcoma consisting of a preparation of doxorubicin encapsulated in liposomes which deliver significantly greater quantities of doxorubicin to the KS lesions while reducing the drug's side effects. DOX-SL incorporates so-called "stealth" liposomes, whose polyethylene glycol (PEG) coating gives them still greater stability in the bloodstream. Side effects include nausea, vomiting, stomatitis, diarrhea and hair loss. DOX-SL causes a significant amount of neutropenia, which can be managed with G-CSF (Neupogen).

Drug-Drug Interaction: The effects that occur when two or more drugs are used together. Such effects include changes of absorption in the digestive tract, changes in the rate of the drugs' breakdown in the liver, new or enhanced side effects and changes in the drugs' activity.

DTH (Delayed-Type Hypersensitivity): A cell-mediated immune reaction to foreign antigen applied on the surface or just under the skin. The reaction takes 24 to 48 hours to develop. DTH, which is the process involved in the reaction to poison ivy and poison oak, is often used in tests of immune system function.

Dyspepsia: Digestive upset, which may include flatulence, heartburn, nausea or vomiting.

Dysphagia: Dysphagia means difficulty with swallowing. The most common cause of dysphagia is an infection by Candida albicans, a fungus that can be easily treated (see Candidiasis, above). Less

frequent causes are infections with herpes or CMV. The usual method of finding the cause of dysphagia is endoscopy, a procedure in which a tube is placed in the esophagus to visualize and biopsy the lesions. X-ray examinations are another means of viewing the esophagus. In many cases, neither of these tests is done, and the person is presumed to have a Candida infection if he or she also has thrush and if swallowing is painful.

Dysphasia: Difficulty speaking.

Dysplasia: Abnormal changes or growth of cells and tissues.

Dyspnea: Shortness of breath or difficulty in breathing.

Dystrophic: Progressive changes that may result from defective nutrition of a tissue or organ.

Early HIV Infection: The stage of HIV infection during which no major physical health symptoms are yet present, though psychological symptoms may be present.

Echinacea: A commonly used herb for maintaining the immune system. There is evidence that use of Echinacea can increase levels of TNF (Tumor Necrosis Factor) which is often already elevated in HIV positive people and may contribute to both wasting and the replication of HIV. Little clinical trial data are available on the herbs value in treating HIV and AIDS.

Eczema: A generic term for various acute or chronic inflammatory conditions of the skin.

Edema: Swelling caused by an abnormal accumulation of fluid in body tissues.

Efficacy: Strength, effectiveness. The ability of a drug to control or cure an illness. Efficacy should be distinguished from activity, which is limited to a drug's immediate effects on the microbe triggering the disease.

Electrocardiography: A method of recording the electrical currents that pass through the heart (muscle) just prior to each heart beat.

Electrocautery: Cauterization (cutting or burning tissue) using electrical current.

Electrocardiogram (EKG): Test used to detect abnormal heart activity by measuring electrical output. Pads with leads going to the electrocardiograph are placed on chest with a gel.

Electroencephalograpm (EEG): Test used to detect electrical or brain wave activity. Pads with leads going to the electroencephalagram are placed on scalp with a gel.

ELISA Test: The ELISA is a blood test done to detect antibodies to certain microbes, among which is HIV. The ELISA is the first of two standard tests done together to detect antibodies to HIV. The test is extremely sensitive but not very specific. Sensitivity means that the test is able to detect HIV infection; specificity means that the test specifically detects a particular infection and no other. In other words, with ELISA, people who have HIV infection will rarely have a falsely negative test, but people who do not have HIV infection can have a falsely positive test. As a result, the ELISA is used

as a screening test, and those who are positive have a second test on the same blood sample called a Western blot.

Elispot: A laboratory method for detecting the presence of HIV.

Empiric Therapy: Treatment based on the clinician's judgment and the patient's symptoms and signs and offered before a diagnosis has been confirmed.

Encephalitis: Encephalitis is an infection of the brain. (Meningitis, by contrast, is an infection of the meninges, the membrane surrounding the brain and spinal cords Meningitis, below.) Encephalitis commonly causes headaches, fever, seizures, and neurologic problems. The diagnosis is frequently made on the basis of the person's symptoms, combined with procedures to examine the brain such as computerized tomography scan (CAT scan) (see above); magnetic resonance imaging (MRI) ; or electroencephalagraph (EEG). Diagnosis can also be made by analyzing the cerebrospinal fluid obtained by a spinal tap . In people with HIV infection, the usual causes of encephalitis are infection with HIV itself or such opportunistic illnesses as toxoplasmosis or lymphoma.

Encephalopathy: A disease of the brain.

Endemic: A chronic incidence of a particular disease in a certain population or region.

Endocrine Gland: One of the organs of the body that reproduces hormones.

Endometrium: The mucous membrane that lines the uterus.

Endoscopy: Endoscopy is a diagnostic procedure in which an instrument is passed through the mouth or rectum to examine an internal organ or to obtain a biopsy (see above). In people with HIV infection, the most common types of endoscopy are bronchoscopy to examine the lungs and endoscopies to examine the digestive system. Upper endoscopy of the intestine involves passing an endoscope through the mouth to examine the esophagus, stomach, or upper small intestine. Lower endoscopy of the intestine involves passing an endoscope through the rectum to examine the large intestine or colon. Endoscopes are flexible and can turn corners. Endoscopy re quires the expertise of a specialist, can be done on an outpatient basis, and usually costs $1,200 to $1,800.

Endpoint: A category of data used to compare the outcome in different arms of a clinical trial. Common endpoints are severe toxicity disease progression or fall in such surrogate markers as CD4 count, but sometimes death is used as an endpoint. Usually when an endpoint reaches a certain set magnitude of change from baseline, a trial participant is removed from the trial and receives an open-label therapy (either a standard treatment or experimental one being tested).

Enteric: Pertaining to the intestines.

Enteritis: Enteritis is an inflammation of the small intestine; the most common symptom is diarrhea. In people with HIV infection, the microbes that usually cause enteritis are cryptosporidia, microsporidia, Mycobacterium avium-intercellulare, and CMV. These microbes can be detected by examining stools under a microscope or with a biopsy of the small intestine done with an endoscope (see above, under Endoscopy), a tube that is placed through the mouth and into the small intestine.

Envelope: The outer covering of a virus, sometimes called the coat.

Env Gene: The gene that encodes spike proteins and glycoproteins of the envelope of HIV.

Enzyme: A protein that can cause chemical changes in other substances without being changed itself.

Enzyme-Linked Immunoabsorbent Assay (ELISA): A laboratory blood test used to detect the presence of HIV and other antibodies.

Eosinophil: Eosinophils play roles in allergic reactions and eliminating parasites; a white blood cell whose granules readily absorb a red stain called eosin.

Eosinophillic Folliculitis: An inflammatory reaction around hair follicles, characterized by very itchy papules that may grow together to form plaques. The cause of this condition in people with AIDS has yet to be established, although the condition obviously involves invasion of the follicles by eosinophils. Partially successful treatment has been reported with ultraviolet light, steroids, antihistamines and itraconazole.

Epidemiology: The study of the frequency, distribution and behavior of a disease in a defined population.

Epidemic: An outbreak of contagious disease, such as HIV infection, that spreads rapidly within a population.

Epithelial: Refers to the cell linings covering most internal and external surfaces of the body and its organs.

Epithelioma (BCE): A carcinoma (malignant growth) of the skin.

Epitope: A unique molecular shape or sequence carried on in a micro-organism that triggers a specific antibody or cellular immune response.

Epogen: A recombinant version of erythropoietin. Used to treat drug-related anemia. There is an identical product, made by another company, called Procrit.

Epstein-Barr Virus (EBV): A herpes-like virus that causes one of two kinds of mononucleosis (the other is caused by CMV). It infects the nose and throat and is contagious. It lies dormant in the lymph glands and has been associated with Burkitt's lymphoma and oral hairy leukoplakia.

Erythropoietin (EPO): A natural hormone that stimulates the production of red blood cells.

Erythrocyte: Red blood cell. The primary function of erythrocytes is to carry oxygen to cells.

Expanded Access: Refers to any of the FDA procedures (compassionate use, parallel track and treatment IND) that distributes experimental drugs to patients who are failing on currently available treatments for their condition and also are unable to participate in ongoing clinical trials.

Experienced: Usually used when referring to a treatment (i.e. "AZT-experienced"). This means a person has taken this drug before.

Extrapulmonary: Outside of the lungs

Famciclovir (Famvir): A prodrug for an acyclovir-like active compound. It has especially high bioavailability and is an approved therapy for shingles. It is also under investigation for herpes simplex-2 (genital herpes).

Family Centered: Describes care that recognizes and respects the pivotal role of the family in the lives of children and other family members. Supports families in their natural care giving roles, promotes normal patterns of living, and ensures family collaboration and choice in the provision of services to members of the family who are sick.

FDA: The Food and Drug Administration, an agency of the US Dept. Of Health and Human Services that regulates the testing of experimental drugs and approves new medical products for marketing based on evidence of safety and efficacy.

Fellatio: Oral contact with the penis; sucking, a blow job, a hummer.

First-line Treatment: The preferred therapy for a particular condition (e.g., trimethoprim-sulfamethoxazole (TMP-SMX) is the first-line treatment for PCP).

Flavanoid: An antioxidant that belongs to a large family of yellow-orange plant pigments

Floater: Drifting dark spot within the field of vision. Floaters can be caused by CMV retinitis, but also can appear in persons as a normal part of the aging process.

Fluconazole (or Diflucan): Fluconazole is used to treat fungal infections, primarily those caused by Candida albicans (thrush or candidal esophagitis) and Cryptococcus neoformans (cryptococcal meningitis). Fluconazole can be taken by mouth or by vein. Side effects are unusual; occasional problems are nausea, rash, or hepatitis.

Fluorescent Treponemal Antibody Absorption Test (FTA-ABS): A treponemal test to detect antibodies against Treponema pallidum, the organism that causes syphilis.

Follicle: A small body cavity with a secretory or excretory function.

Follicular Dendritic Cell (FDC): A special cell in the lymph nodes that helps trap harmful antigens.

Folliculitis: An infection of the hair follicles that occurs most commonly in the hairy areas of the groin, armpit or face, usually due to bacteria.

Foscarnet (Foscavir): An antiviral drug FDA approved to treat CMV infection in the retina and elsewhere in the body. Also has activity against herpes simplex virus, including acyclovir-resistant strains. Possible adverse side effects include kidney toxicity, seizures, anemia, nausea and skin rashes.

Free Radical: A chemically active atom or molecular fragment containing a chemical charge due to an excess or deficient number of electrons. Radicals seek to receive or release electrons in order to achieve a more stable configuration, a process that can damage the large molecules within cells. See oxidation.

Funduscopy: Examination of the interior of the eye with an instrument that permits the examiner to peer into the eyeball through the pupil.

Fundus: A general term for the bottom or base of an organ, such as the stomach or the eye.

Fungal Infections: Infections caused by fungi such as yeast and molds. These infections include thrush, cryptococcal meningitis and Pneumocystis carinii pneumonia (PCP).

Fungus: One of a group of primitive, nonvascular organisms including mushrooms, yeasts, rusts and molds. Some fungi are single-celled but differ from bacteria in that they have a distinct nucleus and other cellular structures. Reproduction is accomplished by spores.

Fusion: A union, by joining together.

Gamma Globulin: See Immunoglobulin G.

Gamma Interferon: A cytokine associated with a cell-mediated immune response.

Ganciclovir (Cytovene): An antiviral drug FDA approved to treat infections caused by cytomegalovirus and occasionally for infections caused by herpes simplex and other viruses. There are both oral and intravenous forms. The oral form has been found to reduce the risk of developing CMV by half in people with advance AIDS. It also delays progression of existing disease, although not to the same extent as the intravenous formulation does. The most important side effect is bone marrow suppression, leading to low white blood cell and platelet counts.

Gastroenteritis: Inflammation of the stomach and intestines, which can cause abdominal pain and diarrhea.

Gastrointestinal: Relating to the stomach and intestines.

G-CSF (Neupogen): Granulocyte colony stimulating factor. G-CSF is a natural hormone that stimulates production of granulocytes, a type of white blood cell. Its synthetic form has been approved by the FDA for prevention of drug-induced neutropenia.

Gene: The biologic unit of heredity; genes contain the genetic or hereditary information encoded by DNA and are located at a unique position in a sequence of genes in the cell's nucleus. Genes determine many aspects of human physiology.

Gene Therapy: Any of a number of experimental treatments in which cell genes are altered. Some gene therapies attempt to provoke new immune activity; some try to render cells resistant to infection; some involve the development of enzymes that destroy viral or cancerous genetic material cells.

Genital Herpes: See herpes simplex virus 2.

Genital Ulcer Disease (GUD): Ulcerative lesions on the genitals, usually caused by a sexually transmitted condition such as herpes, syphilis or chancroid. The presence of genital ulcers may increase the risk of transmitting HIV.

Genital Wart: See Condyloma Acuminatum.

Genome: The genetic code for an entire organism.

Germinal Center: One of a series of follicles or cavities around the periphery of lymph nodes. Germinal centers are the site of antibody production and are populated mostly by B-cells, but include a few T-cells and macrophages. As HIV infection progresses, the germinal centers gradually decay.

Giardia: An intestinal infection caused by a protozoa, that often produces nausea, cramping and diarrhea. Transmission is usually by contaminated water or oral-anal contact.

Gingivitis: A mouth disease which causes gums to become swollen, red, and bleeding. Mostly caused by poor dental hygiene, the buildup of bacterial plaque, diabetes, leukemia, and/or vitamin deficiency.

Gliiosis: A proliferation of certain brain cells and a condition frequently seen in people with HIV-related dementia.

Glucose-6-phosphate Dehydrogenase (G6PD) Deficiency: An inherited enzyme deficiency that can lead to hemolysis of red blood cells (RBCs) when an affected individual is exposed to drugs with oxidant properties.

Glutathione (GSH): A triple amino acid molecule (a tripeptide) utilized in the body as an antioxidant. It helps remove free radicals from blood and cells before they can cause oxidative damage. Glutathione also aids in the neutralization of toxins in the liver. Glutathione levels are comparatively low in people with HIV.

Glycoprotein: A conjugate molecule made up of both protein and carbohydrate components.

Glycyrrhizin: A substance isolated from the root of the licorice plant. Used traditionally as an anti-inflammatory and liver protectant, glycyrrhizin also is thought to have anti-HIV activity. Possible adverse effects include low potassium levels and high blood pressure.

GM-CSF (Leukine, Prokine): Granulocyte-macrophage-colony-stimulating factor. A hormone that stimulates production of both granulocytes and macrophages. Recombinant GM-CSF is under development as a means of alleviating the neutropenia caused by AZT and ganciclovir.

gp41: A glycoprotein from HIV's outside envelopes that complexes with gp120 to form the mechanism enabling HIV to latch onto and enter cells.

gp120: A glycoprotein from HIV's envelope that binds to CD4 molecules on cell's outside membrane. Free gp120 in the body may be toxic to cells on its own, causing CD4 depletion in the immune system through apoptosis and neurological damage leading to AIDS dementia complex.

Gram's stain: A laboratory technique using dyes to identify bacteria.

Granulocyte: A type of white blood cell filled with granules of compounds that digest microorganisms. Granulocytes are part of the innate immune system and have broad-based activity.

They do not respond only to specific antigens as do B-cells and T-cells. Basophils, eosinophils and neutrophils are all granulocytes.

Granulocyte Stimulating Factor (GSF): A natural hormone that stimulates growth of granulocytes, a type of white blood cell. It has been manufactured by genetic engineering (brand names: Neupogen, Filgrastim) and is FDA approved to prevent the neutropenia associated with the use of certain drugs.

Granulocytopenia: An abnormally low number of granulocytes in the blood, which increases the risk of severe bacterial infection.

Griseofulvin (Fulvicin, Grifulvin and others): an antibiotic commonly used to treat superficial fungal infections.

Growth Factor: One of many intracellular regulatory molecules that affect cell proliferation (rapid and repeated reproduction) and maturation in specific tissues.

Guidelines: Clinical practice recommendations made by agreement of experts or based on a literature review by a panel of experts and consumers. Purpose is to educate health care providers, improve the care provided to individuals with specified conditions, and, when possible, enhance the cost effectiveness of health care.

Hairy Leukoplakia: A white lesion seen in the oral cavity of people with HIV. It may be flat or raised and is not removable.

Half-Life: The amount of time required for half of a given substance (such as a drug) or half the current population of a given type cell to be eliminated from the body.

Health Care Facility: A freestanding building (licensed where required) dedicated to the provision of medical and nursing care.

Helminth: An intestinal, worm like parasite.

Helper T-cell: See CD4 cell.

Hematocrit: A test used to measure the percent, by volume, of red blood cells in a particular amount of blood.

Hematologic: Relating to the study of blood.

Hematuria: Red blood cells in the urine.

Hemiparesis: Paralysis on one side of the body.

Hemoglobin: The iron- containing protein in red blood cells that carries oxygen to cells throughout the body. Normal hemoglobin values are 12-15 grams per liter for women and 14-16 grams per liter for men. These normal values may vary according to population and geographic area or region.

Hemolysis: The destruction of red blood cells (RBCs) by drugs, serum proteins (complement), infectious agents, or turbulent blood flow.

Hemophilia: A person with hemophilia lacks a protein that helps the blood to clot. Hemophiliacs bleed easily, even with a minor cut. Hemophilia is inherited, and only by men; Hemophilia has two forms, hemophilia A and hemophilia B; each form lacks a different clotting protein, called a clotting factor.

Hemoptysis: The coughing up of blood from the lungs; may be a symptom of tuberculosis.

Hemorrhage: Bleeding through ruptured or unruptured vessel walls.

Hepatic: Pertaining to the liver.

Hepatitis: Hepatitis is an inflammation of the liver. Many people have no symptoms and are unaware of having hepatitis. The symptoms, when people do have them, are loss of appetite, vomiting, yellow discoloration of the skin and eyes (jaundice), dark urine, sore stomach, and fever. There are different types of hepatitis. Some are caused by a viruses (Hepatitis B that may be transmitted by sexual contact or Hepatitis C that may be transmitted by blood-to-blood transmission). Since these are the same mechanisms of transmitting HIV infection, the same people who are likely to be infected with HIV infection are also likely to be infected with a hepatitis virus. People with HIV infection are also prone to hepatitis caused by CMV and Mycobacterium Avium-Intercellulare. Alcohol and drugs, including AZT, Pentamidine, Ketoconazole, Bactrim, and INH, may also cause liver inflammation. The diagnosis of hepatitis is made with blood tests to determine liver function and to find out the type of hepatitis.

Hepatitis A Virus: A self-limiting virus-induced liver disease. Hepatitis A is acquired through ingesting fecally contaminated water or food or engaging in sexual practices involving anal contact. Injection drug users who share unclean needles are also at risk.

Hepatitis B Virus: The hepatitis B virus is one of the microbes that causes hepatitis. Hepatitis B infection may be acute and cause serious symptoms that last up to a few weeks (see above, under Hepatitis); it may be chronic with occasional symptoms and abnormal liver tests that last for months or years; or it may cause no symptoms at all and may only show up on a blood test. About 5-10 percent of people with hepatitis B infection become chronic carriers of hepatitis B virus. Can cause life-threatening damage to the liver.

Hepatitis C Virus: The hepatitis C virus is another of the microbes that causes hepatitis. Hepatitis C infection may be acute and cause serious symptoms that last up to a few weeks (see above, under Hepatitis); no symptoms at all; and in about 50 percent of cases is chronic with occasional symptoms and progressive liver damage. Some people with hepatitis C infection become chronic carriers of the hepatitis C virus. As with Hepatitis B it can cause life-threatening damage to the liver.

Hepatic Transaminase: Enzymes that transfer amino groups in the liver (the "T" in ALT and AST).

Hepatomegaly: Liver enlargement.

Hepatoxicity: Liver toxicity.

Herpes Simplex Virus-1 (HSV-1): A virus that can cause painful "cold sores" or blisters on the lips

("fever blister") or in the mouth or around the eyes. The symptomatic disease stage occurs at unpredictable intervals of weeks, months or years and is transmittable at this time. The latent (inactive) virus can reactivate due to emotional stress, physical trauma, other infections, or suppression of the immune system. HSV-1 responds well to treatment with acyclovir (Zovirax).

Herpes Simplex Virus-2 (HSV-2): A virus that commonly causes blisters or lesions (sores) on and around the genitals. Herpes simplex is a persistent virus: the virus remains dormant most of the time and then causes recurrent symptoms intermittently over a period of years. The initial infection with herpes simplex virus is often severe with large areas of blisters, occasional fevers, and pain and tingling in the area involved. Subsequent attacks are usually milder. The virus is transmitted to others by contact with the mouth or genitals, especially when the blisters are present.

Herpes Zoster: Herpes zoster is caused by the same virus that causes Chicken pox. The virus stays in the body and may cause symptoms decades after the original infection. Attacks after the first infection are called shingles, or herpes zoster. The skin sores with herpes zoster are similar to those of chicken pox and those of herpes simplex. The sores begin as red spots that become blisters filled with water; the blisters break down into sores with pus, finally scab over, and eventually disappear. Unlike herpes simplex infections or chicken pox, however, the later recurrences of herpes zoster are usually restricted to the area served by a single nerve. In other words, the blisters are restricted to one side of the body, usually in a band across the face, chest, abdomen, back, or leg.

Hickman Catheter: People who need long periods of treatment with specific drugs given by vein will often have a tubing called a Hickman catheter. The catheter is inserted by a specialist, usually a surgeon, through the skin of the chest, and then tunneled under the skin to a vein in the chest. The end of the catheter comes out the chest wall above the breast. Drugs can be injected into the catheter as necessary. The advantage of a Hickman catheter is that it permits access to the vein without repeated needlesticks in the arms. Similar devices are also available (called a port); the Hickman catheter is simply one of the most frequently used. It is important to know that the area around any catheter in a vein can become infected. Symptoms of infection of the area where the catheter comes out are redness and pain, and sometimes pus. Symptom of infection around the catheter inside the body is fever.

Histoplasmosis: An opportunistic infection caused by a fungal infection acquired from inhaling spores of the fungus Histoplasma capsulatum present in soil or dust. The fungus is widespread only in the south-central United States and Latin America. The disease can cause fever, skin lesions, anemia and respiratory distress. Histoplasmosis outside the lungs is an AIDS-defining illness. Amphotericin B and itraconazole are approved treatments.

HIV-1: Human immunodeficiency virus type 1, the retrovirus recognized as the agent that causes AIDS.

HIV-2: Human immunodeficiency virus type 2, a virus closely related to HIV-1 that also leads to immune suppression. HIV-2 is not as virulent as HIV-1 and is epidemic only in West Africa.

HIV Antibody (HIV-Ab): The antibody to HIV, which usually appears within 6 weeks after infection, but could take 6 months or more. Antibody testing early in the infection process may not produce accurate results, since some recently infected people have not yet begun producing antibodies and test negative even though they are infected. Thus, a single negative antibody test result is not a guarantee that a person

is free from infection. The change from HIV-negative to HIV-positive status is called seroconversion.

HIV Counseling: Information provided to an individual before and after HIV testing (pre and post-test counseling) regarding the implications and impact of testing, prevention of HIV transmission and treatment and care if HIV positive.

HIV-infected: Infected with the Human Immunodeficiency Virus, with or without evidence of illness.

HIV-negative: Not infected with HIV, as determined by a negative test for antibody to HIV or for the presence of the virus.

HIV-positive: Infected with HIV, as determined by a positive test for antibody to HIV or for the presence of the virus.

Hodgkin's Disease: A progressive malignant cancer of the lymphatic system. Symptoms include lymphadenopathy, wasting, weakness, fever, itching, night sweats and anemia. Treatment includes chemotherapy and radiation.

Holistic: Comprehensive care; as in physical, social, mental, and emotional health taken together. Also; various systems of health protection and restoration, both traditional and modern, that are reputedly based on the body's natural healing powers, the various ways the different tissues affect each other and the influence of the external environment.

Home Care: Medical care and related services that are given at home by family members, nurses or health care providers, or a combination thereof.

Hormone: An active chemical substance formed in one part of the body and carried in the blood to other parts of the body where it stimulates or suppresses cell and tissue activity (tells different cells what things to do).

Hospice: A facility in which medical and mental health care are provided to a terminally ill patient (usually within six months of death). The hospice philosophy emphasizes alleviating the patient's discomfort and supporting the family in the grieving process.

HPMPC: See Cidofovir.

Human Growth Hormone: A peptide hormone secreted by the anterior pituitary gland in the brain; enhances body growth by stimulating carbohydrate and protein metabolism.

Human Immunodeficiency Virus (HIV): The organism isolated and generally recognized as the cause of AIDS. HIV is classified as a lentivirus in a subgroup of the retroviruses. It infects and destroys a class of lymphocytes, CD4 cells, thereby causing progressive damage to the immune system.

Human Papilloma Virus (HPV): A member of the papova family of viruses. HPV causes wart-like bumps on the genitals, anus or cervix. HPV has been associated with cervical cancer in women and anal cancer in men.

Humoral Immunity: The immune response that is mediated by B cells and involves production of antibodies. Humoral immunity (also known as TH-I immune response) is associated with the production of the cytokines interleukin-4 and interleukin-10.

Hydrate: A crystalline compound composed of one or more molecules of water.

Hydrocortisone: Synthetic cortisone in a cream formulation used to reduce skin inflammations; a hormone (also called cortisol) excreted by humans in small amounts.

Hydrogen Peroxide: A chemical normally produced by a cell to destroy unwanted molecules such as waste products within the cell; also is a liquid used to disinfect a cut or wound.

Hydroxyurea: An approved oral chemotherapeutic agent for leukemia and ovarian cancer. It is an experimental anti-HIV treatment. Hydroxyurea blocks the action of the cellular enzyme ribonucleotide reductase, which helps produce the nucleotides needed for DNA formation. By reducing the amount of functioning nucleotides, the compound makes intracellular HIV more sensitive to the defective nucleoside analogs. Hydroxyurea has been found to be particularly synergistic with ddI in lab tests.

Hypergammaglobulinemia: Abnormally high blood levels of immunoglobulins (antibodies).

Hyperpigmentation: Increased coloration of the skin. Can be caused by drugs, including Bactrim.

Hyperplasia: Excessive growth of normal cells.

Hypertension: High blood pressure.

Hypericin: A compound derived from the herb St. John's wort. It is an experimental treatment for HIV and human papillomavirus (HPV). Hypericin inhibits the assembly and shedding of virus particles in infected cells. A synthetic version has been developed. Hypericin's main side effect is extreme photosensitivity.

Hyperthermia: An experimental procedure that involves temporarily heating a patient's body core to temperatures of up to 108 degrees F on the theory that this temperature kills free HIV and HIV-containing cells. One method for accomplishing this is by passing patient's blood through an external heater. This is called extracorporeal whole body hypothermia. There is not sufficient data to support the benefits of this treatment. It may be very dangerous. It is costly.

Iatrogenic: Refers to an unfavorable response to medical or surgical treatment that has been induced by the treatment itself.

Idiopathic CD4 T-Lymphocytopenia (ICL): Immune deficiency defined by CD4 count of below 300 without HIV.

Idiopathic Thrombocytopenic Purpura (ITP): A low number of platelets in the blood, which is common in people with HIV, but often resolves as immune deficiency worsens. HIV-related ITP usually does not have serious consequences. Its cause has not been definitely determined. Treatment with AZT frequently alleviates the condition.

IL-1 (Interleukin-1): A cytokine that is released early in an immune system response by monocytes and macrophages. It stimulates T-cell proliferation and protein synthesis. Another effect of IL-1 is that it causes fever. See also Interleukin.

IL-2 (Interleukin-2): A cytokine secreted by Th1 CD4 cells to stimulate CD8 cytotoxic T-lymphocytes. IL-2 also increases the proliferation and maturation of the CD4 cells themselves. During HIV infection, IL-2 production gradually declines. Use of IL-2 therapy is under study as a way to raise CD4 cell counts and restore immune function. See also Interleukin.

IL-4 (Interleukin-4): A cytokine secreted by the Th2 CD4 cells that promotes antibody production by stimulating B-cells to proliferate and mature. See also Interleukin.

IL-6 (Interleukin-6): A cytokine whose production affects many different cells in the immune system. See also Interleukin.

IL-12 (Interleukin-12): A cytokine released by macrophage in response to infection that promotes the activation of cell-mediated immunity. Specifically, IL-12 triggers the maturation of Th1 CD4 cells, specific cytotoxic T-lymphocyte responses and an increase in the activity of NK cells. IL-12 is under study as an immunotherapy in HIV infection. See also Interleukin.

Immune Deficiency: A breakdown or inability of certain parts of the immune system to function, thus making a person susceptible to certain disease that they would have not contracted with a healthy immune system. Immune deficiencies may be temporary or permanent and be triggered by genetic mutation, therapy with immunosuppressive drugs (as during organ transplants) or an infections such as HIV.

Immune System: The body's complicated natural defense against disruption caused by invading microbes and cancers. There are two aspects of the immune system's response to disease: innate and acquired. The innate part of the response is mobilized very quickly in response to infections and does not depend on recognizing specific proteins or antigens foreign to an individual's normal tissue. It includes complement, macrophages, dendritic cells and granulocytes. The acquired, or learned, immune response arises when dendritic cells and macrophages present pieces of antigen to lymphocytes, which are genetically programmed to recognize very specific amino acid sequences. The ultimate result is the creation of cloned populations of antibody-producing B-cells and cytotoxic T-lymphocytes primed ton respond to a unique pathogen.

Immunofluorescence Antibody (IFA): A serologic assay using antibody tagged by a fluorescent molecule. There is an HIV-specific IFA assay available to confirm the results of a positive HIV ELISA test.

Immune Modulator: A substance that modifies immune functions; the term generally used to identify substances that enhance immune functions. This includes two sub-groups: cytokines and "broad acting" immune modulators. Cytokines are proteins made by immune cells that influence other immune cells (e.g. the interleukins-2,4,5,10 and 12). "Broad-acting" immune modulators are chemical transmitters/hormones in the body that regulate the immune system (e.g., endorphins).

Immunization: Administration of antigenic components of an infectious agent to stimulate a protective immune response.

Immunity: Natural or acquired resistance to a specific disease. Immunity may be partial or complete, long lasting or temporary.

Immunodeficiency: A breakdown or an inability of certain parts of the immune system to function that renders a person susceptible to certain diseases that he or she ordinarily would not develop.

Immunocompetent: Refers to an immune system capable of developing a normal protective response when confronted with invading microbes or cancer.

Immunocompromised: Describes the condition that exists when the body's immune system defenses are lowered and the ability to resist infections and tumors weakens.

Immunoglobulin (Ig): Protein produced by plasma cells derived from B-lymphocytes and found in the blood and other body tissues. Increased levels of two types of immunoglobulins, IgA and IgG, are usually seen in patients with HIV infection and are related to the HIV-induced activation of B-lymphocytes. Immunoglobulin A is found in high concentrations in mucous membranes and in secretions such as saliva. It does not cross the placenta. Immunoglobulin G is found in the serum and does cross the placenta.

Immunoblastic Lymphoma: An AIDS defining opportunistic infection caused by a cancerous growth or tumor. It is diagnosed by X ray, CAT scan, MRI or biopsy.

Immunosuppression: Weakening of the immune system response that occurs with HIV infection as well as with some antiviral or anticancer treatments.

Immunotherapy: Treatment aimed at reconstituting an impaired immune system. Examples of experimental immunotherapies for AIDS include passive hyperimmune therapy (PHT), IL-2 and therapeutic vaccines.

Incubation Period: The incubation period of a disease is the time interval between infection with a microbe and the first symptoms of disease. For influenza and common colds, the incubation period is usually several days; for measles, chicken pox, mumps, and infections caused by many other viruses, the incubation period is two to three weeks. An unusual feature of HIV infection is that the first symptoms of a weakened immune system usually do not occur until several years after the infection takes place.

Indication: Purpose for which a drug is prescribed. The FDA approved indications appear on a printed insert included with the manufacturer's drug packaging.

IND Status: Investigational new drug status; an FDA classification that makes certain drugs available to individuals on a case-by-case basis. See Investigational New Drug.

Informed Consent: The ability of people receiving services (i.e. HIV antibody test, certain medical procedures (like an operation), participation in a clinical trial to make competent decisions about their medical care. Before taking the test, undergoing the procedure, or participating in the trial, the person or the person's representative must sign an informed consent form stating that he or she has been informed about the purpose, benefits, risks, and alternatives to the test, procedure, or trial, and that he or she consents to it. In the case of participation in a clinical trial, the informed consent form explains the purpose of the trial, what will be done, the risks of participation, the benefits of participation, what other treatments are available, and the right of the participant to leave the trial at any time.

Influenza Vaccine: The influenza vaccine varies in effectiveness, depending on whether the strain of virus in the vaccine is related to the virus which is causing the influenza. The effectiveness of the vaccine changes every year. In most years, however, the vaccine probably prevents about 70 percent of the cases of influenza, and those who become infected despite having been vaccinated usually have less severe symptoms. Influenza does not seem to be unusually common or severe in people with HIV infection. The only problem specific to people with HIV infection is that the symptoms of influenza can be confused with the symptoms of pneumonias such as Pneumocystis pneumonia (see Pneumocystis carinii, below). Therefore, the CDC's Advisory Committee on Immunization Practices recommends that people with HIV infection routinely get the influenza vaccine every year.

Infusion: The process of giving a substance to an individual by injecting it into a vein. This procedure can either be a one-time event or continued over many hours, days or even months.

Inoculum Size: Inoculum size is a term used in the field of infectious diseases to describe the number of microbes necessary to cause an infection. In HIV infection, for example, a certain number of viruses is required before infection takes place. The specific number is not known. What is known is that the probability of transmitting HIV with the transfusion of one unit (or 500 milliliters) of infected blood is 80 to 90 percent. The probability of transmitting HIV with a needlestick injury, which injects only a fraction of a milliliter of blood, is 0.4 percent. This difference in the probabilities of transmission is most likely due to differences in inoculum size.

Institutional Review Board (IRB): A regulating committee composed of internal staff, hospital affiliates and community members which reviews and approves all human trials conducted within a particular hospital or research center. The IRB ensures that a trial is conducted in an ethical manner, with proper protection of human subjects.

Integrase: The HIV enzyme that insert's HIV's genes into a cell's normal DNA. Integrase operates after reverse transcriptase has created a DNA version of the RNA form of HIV genes present in virus particles. Drugs that block the action of integrase are under development.

Interferon: One of a number of antiviral proteins that modulate the immune response. Interferon alpha is secreted by a virally infected cell and strengthens the defenses of nearby uninfected cells. A manufactured version of Interferon alpha (trade names: Roferon, Intron A) is an FDA approved treatment for KS, hepatitis B and C viruses. Interferon gamma is synthesized by immune system cells (NK cells and CD4 cells). It activates macrophages and helps orient the immune system to a mode that prompts cellular immunity (Th1 response). The major side effects of interferons are the aches and fever that accompany flu: it is the interferon produced by the body that causes these symptoms during flu.

Interim Analysis: An intermediary analysis of clinical trial data, performed at a point at which enough data have been gathered top derive preliminary, but not necessarily complete conclusions. Interim analyses are performed to see whether continuation of a clinical trial is warranted.

Interleukin: One of a large group of glycoproteins that act as cytokines. The interleukins are secreted by and affect many different cells in the immune system.

Interstitial Pneumonia: Chronic inflammation of the lungs. (See lymphoid interstitial pneumonia).

Intolerant: Unable to take a drug because of an adverse reaction (side effect).

Intralesional: Occurring in or introduced directly into a localized lesion.

Intramuscular (IM): Injected directly into a muscle.

Intraocular: Injected into the eye.

Intrathecal: Injected directly into the spinal canal.

Intravenous (IV): Within or into the veins. Intravenous drugs are injected directly into the veins.

Intravenous Immunoglobulin (IVIG): A sterile solution of concentrated antibodies extracted from healthy people. IVIG is used to prevent bacterial infections in people with low or inappropriate antibody production. Injected into a vein or muscle.

Intravitreal: Injected into the eye's vitreous humor between the lens and the retina.

Investigational New Drug (IND): Status given an experimental drug after the FDA approves an application for testing it in people.

In Vitro: Testing and experiments conducted in a laboratory setting (i.e. test tube or culture plate).

In Vivo: Testing and experiments conducted in animals or humans, in a living, natural environment.

Isolate: In microbiology and virology, a specific strain of a particular microbe (In Vivo strains of HIV-1).

Isoniazid (INH): Isoniazid is the standard drug used to treat and prevent tuberculosis. Isoniazid is usually recommended for any person with HIV infection who has tuberculosis or who has a positive tuberculosis skin test. The usual dose is 300 milligrams, taken by mouth. The most important side effect is hepatitis, including jaundice (yellowish skin and eyes), dark urine, nausea, peripheral neuropathy and abdominal pain. This side effect is more likely in people who already have liver damage for other reasons, and in older people. People taking isoniazid and having these symptoms should stop taking the drug immediately and call their physician.

Isosporiasis: An AIDS defining opportunistic infection caused by the parasite isospora belli. Its symptoms include diarrhea, abdominal pain, and weight loss. It is diagnosed by microscopic examination of stool sample.

-its: A suffix that indicates inflammation, usually due to infection, of the root word. For example, vaginitis means inflammation of the vagina.

Itraconazole (Sporanox): Oral antifungal drug used for a number of AIDS related fungal infections. Itraconazole concentrates in the skin and is particularly effective for skin conditions. Possible side effects include digestive upset, loss of potassium and headache.

Jaundice: Yellow pigmentation of the skin and whites of the eyes caused by elevated blood levels of bilirubin. The condition is associated with either liver or gallbladder disease or excessive destruction of red blood cells.

Kaposi's Sarcoma: Kaposi's sarcoma is an AIDS defining illness consisting of individual cancerous lesions caused by an overgrowth of blood vessels. Next to Pneumocystis pneumonia, it is most likely to be the first AIDS-defining diagnosis that men with HIV have; approximately 20 percent of all people with AIDS have Kaposi's sarcoma. The symptoms of Kaposi's sarcoma are pink or purplish painless spots or nodules, a quarter of an inch to an inch in diameter, usually appearing anywhere on the skin. The nodules will grow in size and number. They sometimes occur on internal organs like the lung, brain, and gastrointestinal tract, and in this case is life-threatening. There has been considerable speculation that KS is not a spontaneous cancer but is sparked by a virus. A species of herpes virus similar to Epstein-Barr virus is currently under investigation. Up to now, KS has been treated with alpha interferon, radiation therapy (*outside* the oral cavity) and various systemic and intralesional cancer therapies.

Karnofsky Performance Score: A measure given by a physician to a patient's ability to perform certain ordinary tasks: 100-normal; no complaints; 70 - unable to carry on normal activity; 50 - requires considerable assistance; 30 - disabled; 30 - hospitalization recommended.

K-Cell: A type of nonspecific lymphocyte that seeks out and kills any cells coated with antibody. (The cells become coated because they are infected with virus and contain viral proteins on their surface membranes).

Ketoconazole (Nizoral): Ketoconazole is a drug given by mouth (pill and liquid) for infections caused by Candida albicans and other fungi (oral, esophageal and vaginal candidiasis and cryptococcosis). Ketoconazole requires acid in the stomach to be absorbed into the system. People should therefore not take other medicines that neutralize stomach acids until at least two hours after the dose of ketoconazole. Side effects include nausea, vomiting, hormonal problems (menstrual problems and reduced sex drive due to reduced testosterone levels), rash, headaches, and liver damage.

Killer Cell: A generalized name for immune system cells that kill cancerous and virus-infected cells. Among the killer cells are killer T-cells (cytotoxic T-lymphocytes), NK (natural killer) cells and K-cells.

Killer T-Cell: See Cytotoxic T-Lymphocyte.

Lactose Intolerance: The inability to digest milk products due to the lack of the enzyme lactase, which breaks down milk sugar (lactose).

Langerhans Cell: The type of dendritic cell found in the skin. See Dendritic cell.

Latency: Latency and dormancy (which literally means sleeping) mean the same thing: a microbe is in the body but is not actively reproducing, not invading any tissues, and not causing symptoms. Examples of microbes that are latent or dormant in many or most healthy people are: Pneumocystis carinii, toxoplasma gondii, herpes simplex virus, the virus that causes herpes zoster, and cytomegalovirus. Once in the body, these microbes remain in the body. They remain latent or dormant until something tilts the balance in the immune system and permits them to become active.

L-Carnitine: A naturally occurring cell constituent that modulates fat metabolism, in particular the mitochondrial intake of lipid derivatives. L-carnitine had been proposed as a treatment for AIDS-related wasting and the myopathy associated with AZT.

Lesion: Any abnormal change in tissue caused by disease or injury.

Leukocyte: Any of the various white blood cells, which together make up the immune system. Neutrophils, lymphocytes and monocytes are all leukocytes. Some can move from the bloodstream to tissue and back again. Most leukocytes act as scavenger cells.

Leukocytosis: An abnormally high number of leukocytes in the blood. This condition can occur during many types of infection and inflammation.

Leukopheresis: A procedure in which leukocytes are removed from blood that has been withdrawn from a donor; the remainder is returned to the donor.

Leukopenia: Leukopenia means a low number (or penia) of white blood cells (or leukocytes; leuko means white), the cells of the immune system that fight infection. Leukocytes include lymphocytes (cells that recognize foreign material) and neutrophils (cells that gobble up microbes). The normal leukocyte count is 4,000 to 8,000 per milliliter of blood. In people with certain infections, especially with bacterial infections, the leukocyte count is high (leukocytosis). In people with viral infections, including HIV infection, the leukocyte count is low (leukopenia); having a low count of lymphocytes is called lymphopenia; lymphopenia is the expected result of HIV infection. A low count of neutrophils is called neutropenia; neutropenia can be caused by HIV itself or by some of the drugs commonly taken during HIV infection. Neutropenia becomes worrisome if the count is less than 750 per milliliter; if the count is less than 500 per milliliter, the person is prone to bacterial infections.

Leucovorin calcium: A calcium salt of folic acid (a member of the vitamin B complex). Leucovorin is used to treat severe anemias. The effectiveness of leucovorin calcium as a supplement to treatment with TMP-SMX is not well understood, but it has been shown to reduce the toxicity of other drugs, e.g., trimetrexate, a drug sometimes used to treat Pneumocystis Carinii pneumonia (PCP).

Licorice: See Glycyrrhizin.

Lipase level: Enzymes in the digestive system which break down fat.

Lipids: Biomolecules that are insoluble in water; extracted from animal and plant cells by use of organic chemical "fat" solvents.

Liposome: Microscopic globules of lipids manufactured to enclose medications. The liposome's fatty layer is supposed to protect and confine the enclosed drug until the liposome binds with the outer membrane of target cells. By delivering treatments directly to the cells needing them, drug efficacy may be increased while overall toxicity is reduced.

Liquid Nitrogen: The liquid form of nitrogen, N2, used to freeze things, such as tissue, quickly and at very low temperatures.

Liver Enzyme: See both ALT and AST.

Liver Function Test (LFT): A test that measures the blood serum level of any of several enzymes produced by the liver. An elevated liver function test is a sign of possible liver damage.

Log (logarithm): Formally, the number of times ten must be multiplied with itself to equal a certain number. For example 100,000 is log 5 because it is equal to 10 X 10 X 10 X 10 X 10. Logs are used to measure changes in viral load. For example, a reduction in viral load from 100,000 to 1,000 copies/ml is a two log (or 99%) reduction. Note that a half log change is not a five-fold difference but a change of 3.16 fold (the square root of ten).

Long Terminal Repeat (LTR): The genetic material at each end of the HIV genome. When the genome is integrated into a cell's own genome, the LTR interacts with cellular and viral factors to trigger the transcription of the HIV integrated HIV DNA genes into an RNA form that is packaged in new virus particles. Activation of LTR is a major step in triggering HIV replication.

Long-Term Nonprogressor: An individual who has been infected for at least seven to twelve years (there is no consensus on time span) and yet retains a CD4 cell count within the normal range.

Long-Term Survivors: While there is no consensus on the length of time, generally refers to people with HIV that live for a long period of time.

Loviride: See NNRTI.

Lumbar puncture (LP): Insertion of a needle into the spinal canal to obtain a sample of cerebrospinal fluid. Also called a spinal tap.

Lymph: A clear fluid in lymph vessels that carries lymphocytes and collects foreign microbes. Lymph is derived from tissue fluids. The fluid passes through the lymphatic ducts and then enters the bloodstream. Lymphocytes, which are a part of the immune system, circulate in the lymph.

Lymph Node (Lymph Glands): Small, bean-sized organs made up mostly of lymphocytes, lymph fluid and connective tissue. Clusters of lymph nodes are widely distributed in the body and are essential to the functioning of the immune system. They are connected with each other and other lymphoid tissue by the lymphatic vessels.

Lymphadenopathy: Swollen lymph glands. They are most common at the back of the neck, along the jaw, in the armpits, and in the groin. The lymph glands may feel like rubbery, discrete nodules that are rarely tender to touch and often bean-sized; glands of this description are common in everyone and in several conditions unrelated to HIV infection. If they are swollen to abnormal size for longer than a month in at least two different areas, they constitute persistent generalized lymphadenopathy (PGL).

Lymphatic Vessel: One of a body-wide network of channels similar to the blood vessels, that transports lymph to the lymphoid tissue and into the bloodstream.

Lymphocyte: White blood cells that mature and reside in the lymphoid organs and are responsible for the acquired immune response (see Immune System). The two major types of lymphocytes are T-cells and B-cells.

Lymphoid Interstitial Pneumonitis (LIP): A type of pneumonia that affects 35 to 40 percent of children with AIDS and causes hardening of the lung membranes involved in absorbing oxygen. LIP is an AIDS-defining illness in children.

Lymphoid Tissue: The organs of the body, including the bone marrow, thymus, lymph nodes, spleen, tonsils, Peyer's patches and the lymphocyte aggregates on mucosal surfaces.

Lymphokine: A substance produced by lymphocytes to precipitate various immune reactions. Lymphokines include the interferons and interleukins and are a subset of the cytokine family.

Lymphoma: A cancer of the lymphatic system. About 1 to 3 percent of people with AIDS have lymphomas, and for people with AIDS, lymphomas are classified as opportunistic tumors. There are many types of lymphomas: some progress extremely slowly, cause few symptoms, and require minimal treatment; some are more severe. People with AIDS generally have lymphomas called non-Hodgkin's lymphomas of B cell origin. These lymphomas tend to be severe, and they also tend to involve unusual areas of the body like the brain, liver, kidneys, intestines, and lungs. The diagnosis is usually established with a biopsy. Treatment is variable and often requires the assistance of a specialist in cancer treatment using cancer chemotherapy or radiation treatment.

Lymphoproliferative Response: A specific immune response that entails rapid T-cell replication. Standard antigens, such as tetanus toxoid, that elicit this response are used in lab tests of immune competence.

Lysis: The splitting and dissolution of cellular or viral material by chemical action.

Mycobacterium Avium Complex (MAC) or Intercellulare (MAI): A serious AIDS defining opportunistic infection caused by two similar bacteria (Mycobacterium *avium* and *Mycobacteria Intercellulare)* found the soil and dust particles. In AIDS, MAC can spread through the bloodstream to infect lymph nodes, bone marrow, liver, spleen, spinal fluid, lungs and intestinal tract. Its symptoms may include fever, night sweats, weight loss, diarrhea, fatigue and enlarged spleen. It is diagnosed by biopsy, culture, blood test and emanation of stool sample. MAC usually does not occur until people have CD4 counts below 100.

Macrophage: A large scavenger cell that ingests degenerated cells, blood tissue and foreign particles, and secretes messenger proteins (monokines) involved in inflammatory reactions, lymphocyte activation and acute systemic immune responses. Macrophages exist in large numbers throughout the body and are key to the development of immunity to a variety of organisms. Along with their precursor blood cell, the monocyte, macrophages are a major reservoir of HIV infection.

Macula: The pigmented central area or "yellow spot" of the retina that is adjacent to the optic nerve. It is the most sensitive area of the retina and contains the fovea, a depressed region that is responsible for detailed central vision.

Magnetic Resonance Imaging (MRI): A non-invasive, non-x-ray diagnostic technique based on the magnetic fields of hydrogen atoms in the body. MRI provides computer-generated images of the body's internal tissues and organs. The person getting an MRI is placed inside a large tubular structure and remains motionless for thirty to sixty minutes. During that time, the person's body is bathed in a magnetic field, which causes the atoms in different tissues to give off tiny radio signals. The signals are different depending on the kind of tissue. An MRI is better than a CAT scan at detecting diseases of the brain and spinal cord. MRI is painless, harmless, and does not involve exposure to radiation; the body is not exposed to any kind of potentially harmful radiation. MRIs are also expensive, from $500 to $1,000.

MAI (Mycobacterium Intercellulare): See MAC.

Maintenance Therapy: Extended drug therapy, usually at a diminished dose, administered after a disease has been brought under control. Maintenance therapy is utilized when a complete cure is not possible, and a disease is likely to recur if therapy is halted.

Major Histocompatibility Complex (MHC): Two classes of molecules on cell surfaces. MHC class I molecules exist on all cells and hold and present foreign antigens to CD8 cytotoxic T-lymphocytes if the cell is infected by a virus or other microbe. MHC class II molecules are found on the immune system's antigen presenting cells and display antigen to activate CD4 T-helper cells.

Malabsorption: Inability of the intestines to absorb food, drug or any substance needed to maintain good health.

Malaise: A vague feeling of discomfort or uneasiness, often the result of infection or a drugs side effects.

Malignant: Used to describe cells or tumors growing in an uncontrolled fashion, either spreading to other sites through the blood stream or invading nearby, normal tissues. By definition, cancers are always malignant, and the term "malignancy" implies a cancer.

Malnutrition: Faulty nutrition resulting from poor diet, under eating, or abnormal absorption of nutrients from the gastrointestinal tract.

Mandatory Reporting: System under which a physician is required by law to inform health authorities when a specified illness is diagnosed. Mandatory reporting is required for AIDS in all 50 States, and it has been proposed that the requirement be extended to HIV infection.

Manifestation: The outward sign that an illness is present - a symptom or condition.

Marinol (Dronabinol): An appetite stimulant produced from THC, the active ingredient in marijuana.

Mast Cell: An immune system cell filled with granules of inflammatory chemicals such as histamine. This cell is believed to play a leading role in generating the symptoms of allergy.

Medicaid: Federal/State health care program for persons below the poverty level.

Medicare: Federal health insurance program for persons 65 years of age and older, the disabled, and those with end-stage renal disease.

Medulla: The inner portion of an organ.

Megadosing: Medical treatment with very large doses of a nontoxic substance, usually a vitamin.

Megestrol Acetate (Megace): An appetite stimulant approved for the treatment of weight loss in people with AIDS. The drug has virtually no serious side effects, even with doses as high as 800 milligrams daily. Megestrol Acetate is a synthetic version of the female hormone progesterone.

Melanoma: A type of cancer derived from cells capable of forming melanin, such as skin cells. The

occurrence of melanoma is increasing significantly in the general population and is associated with exposure to sunlight and other ultraviolet light.

Membrane: A thin sheet or layer of pliable tissue (or lipids in the case of cells) serving as a semi-permeable covering.

Memory T-Cell: A T-cell that bears receptors for a specific foreign antigen encountered during a prior infection or vaccination. After an infection or a vaccination, some of the T-cells that participated in the response remain as memory T-cells, which can rapidly mobilize and clone themselves should the same antigen be re-encountered during a second infection at a later time.

Meningitis: Meningitis is an infection or inflammation of the meninges, the membrane that envelopes the brain and spinal cord. It may be caused by a bacterium, fungus or virus. The most common cause of meningitis in people with HIV infection is Cryptococcus (see cryptococcosis, above).

Meprobamate (e.g., Equanil, Miltown): A drug that acts on the central nervous system much as barbiturates do. Meprobamate is used most commonly to treat anxiety. Meprobamate can cause drowsiness, lethargy, and lack of coordination. Continued use may cause psychological and physical dependence. Withdrawing the drug suddenly after prolonged, regular use may cause severe withdrawal symptoms.

Metabolic: Refers to the process of building the bodies molecular structures from nutrients (called anabolism) and of breaking them down for energy production and excretion (called catabolism).

Methadone Hydrochloride: An opiate that is commonly used to control narcotic withdrawal symptoms; in persons with AIDS it is sometimes used to control pain. Methadone can be given by mouth or by vein. Side effects are those shared by all morphine-like drugs that depress the central nervous system: dizziness, mental clouding, depression, and sedation. Methadone may cause physical dependence. If it is stopped abruptly after prolonged and regular use, it can cause withdrawal symptoms.

Metronidazole (e.g., Flagyl): An antibiotic taken by people with HIV for common intestinal infections and common dental problems like gingivitis (inflammation of the gums) and Periodonitis (infection of the structures that support the teeth). Side effects are unusual, primarily nausea and stomach pain. Taking this drug for periods of months may cause pain in the feet that resembles the pain of HIV neuropathy . This pain usually goes away when the drug is stopped.

MHC: See Major Histocompatibility Complex.

Microbes: Living organisms so small they require a microscope to be seen. They can be bacteria, viruses, parasites, or fungi. Microbes cause infectious diseases. The microbes that commonly cause the opportunistic infections that accompany HIV infection are as follows: *Viruses;* Cytomegalovirus, herpes simplex, herpes zoster, molluscum contagiosum, *Bacteria;* Mycobacterium avium-intercellulare, Mycobacterium tuberculosis (the cause of tuberculosis), Salmonella, Nocardia, *Parasites;* Toxoplasma gondii, Pneumocystis carinii, Cryptosporidium, Isospora, *Fungi;* Cryptococcus, Histoplasma, Candida albicans

Microhem Agglutination Assay for T. Pallidum (MATP): A treponemal test for syphilis based on agglutination of red cells to which antigens from the micro-organism T. pallidum have been attached.

Micronutrient: A vitamin or mineral that the body must obtain from outside sources. Micronutrients are essential to the body in small amounts because they are either components of enzymes (the minerals) or act as coenzymes in managing chemical reactions. See also vitamin.

Microsporidium: A protozoa parasite that causes microsporidiosis, a cause of diarrhea and wasting in people with HIV.

Microsporidiosis: An AIDS defining opportunistic infection caused by two different species of the protozoa Microsporidia. It is an infection of the intestines, liver, muscles and cornea diagnosed. It is diagnosed by stool sample, biopsy, and/or visual exam of the eye.

Mineral: An inorganic substance lacking carbon needed by the body for proper nutrition and intracellular metabolism.

Mites: Any of numerous small disease-carrying arachnids that often infest animals, plants and stored foods.

Mitochondria: A rod-shaped or oval body in cells that is the site of energy production by means of oxidation.

Mitogen: A substance that induces cell division.

Molluscum Contagiosum: A small, round, raised, dome-shaped lesion of the skin caused by the pox virus; lesions usually appear on the face, neck, arms, legs and in the anogenital region. This condition is difficult to manage in HIV disease. Current treatments include liquid nitrogen to freeze lesions or curation (cutting out) of the lesions.

Monoclonal Antibody: An antibody produced by laboratory cultures of a single cell line. The antibodies all bind with the same antigen on a bacteria, virus or cancer cell and are supposed to evoke an immune response.

Monocyte: A type of large, white blood cell that leaves the bloodstream to become a macrophage; one of the reservoirs for HIV.

Mononeuritis Multiplex (MM): A rare type of neuropathy that causes patchy areas of movement and asymmetrical sensory abnormalities. MM tends to occur during the asymptomatic, early period of HIV infection, but a more severe type, attributed to CMV infection, has been observed in people with advanced AIDS.

Monotherapy: Use of a single drug administered alone for treatment.

Morbidity: Affected by disease.

Mucous membranes: A moist layer of tissue lining the digestive, respiratory, urinary and reproductive tracts (most body cavities that have openings to the external world, except the ear canals).

Multiple Drug Resistant Tuberculosis (MDR-TB): A strain of TB that does not respond to two or more standard anti-TB drugs. MDR-TB usually occurs when treatment is interrupted thus allowing

mutations in the organism to occur that confer drug resistance. People can also be infected by TB that is already drug resistant.

Mutation: A change in the character of a gene that is perpetuated in subsequent cell divisions.

Myalgia: Pain in one or more muscles

Mycobacterium: A group of organisms that may cause disease, especially in people with poor immunity; includes the causative organisms for tuberculosis (M. tuberculosis), leprosy and MAC.

Mycobacterium Avium Complex (Mycobacterium Intercellulare): See MAC.

Mycoplasma: A microorganism, of which there are many varieties, some of whose members cause disease in animals and humans. Typically, they don't cause problems for people with healthy immune systems. Mycoplasma are very simple, one-celled, wall-less organisms that penetrate and infect individual cells.

Mycobacterium Tuberculosis: The micro-organism that causes tuberculosis.

Mycosis: Any disease caused by a fungus.

Myelosuppression: The suppression of bone marrow activity, causing decreased production of red blood cells (anemia) or white blood cells (leukopenia). Myelosuppression is an effect of some drugs, such as AZT.

Myelitis: Inflammation of either the spinal cord or the bone marrow.

Myelopathy: Any disease affecting the spinal cord.

Myelotoxic: Destructive to the bone marrow.

Myocardial: Refers to the heart's muscle mass.

Myopathy: Progressive muscle weakness. Myopathy may arise as a toxic reaction to AZT or as a consequence of HIV infection itself.

National Institutes of Health (NIH): A federal organization located in Bethesda, Maryland, that funds scientific research. The NIH is the world's largest research organization, with a budget of over $10 billion a year. The NIH is divided into fifteen different institutes, each with a different scientific specialty: the National Institute for Allergy and Infectious Diseases (NIAID) is responsible for most of the research into HIV infection.

N-Acetylcysteine (NAC): A naturally occurring substance that is metabolized into the amino acid cysteine. Cysteine is one of the three components of the major cellular antioxidant glutathione, and people with HIV nave decreased levels of this compound. Clinical studies of oral and intravenously administered NAC are evaluating its usefulness in decreasing HIV activity. See also oxidative stress.

Naive: Usually used when talking about a specific treatment (i.e. "AZT naive"). It means a person has not taken this drug before.

Naive T-Cell: A T-cell arising from the immune system's production of fresh cells in the bone marrow. Naive T-cells respond to newly encountered pathogens containing antigens the immune system has not processed before. The naive T-cells' activation and proliferation create an acquired immune response to the newly encountered pathogenic agent. After the disease is eradicated, a portion of the T-cell population engendered by the activated naive T-cell constitutes a reservoir of memory cells, which proliferate and respond very quickly to any recurrence of the disease. See both Memory T-cell and Immune System.

Natural Killer (NK) Cell: A type of lymphocyte (white blood cell) that attacks and destroys foreign, infected and cancerous cells. NK cells are not targeted at specific antigens the way cytotoxic T-lymphocytes are.

Nausea: The urge to vomit.

NDA (New Drug Application): .After completing Phase III clinical trials and before a drug can be released for over-the-counter sale, a drug sponsor must file an NDA with the FDA. The FDA review process for an NDA usually takes 6 months to a year.

Nef: An HIV regulatory protein whose functions are not well understood. HIV without Nef appears to be less infectious.

Neopterin: A substance present in bodily fluids that is elevated when the immune system is activated. Serum neopterin levels are measured in some studies as an additional (or complementary) surrogate marker for HIV disease. According to some studies, high neopterin levels have been associated with a poor prognosis; low levels have correlated with a better prognosis.

Nephrotic Syndrome: One type of disease or failure of the kidneys.

Nerve: A cord like structure composed of a collection of fibers that conduct impulses between one part of the central nervous system to some other part of the body.

Nerve Growth Factor (NGF): A naturally produced substance that has many roles in the maintenance of nerves and nerve cells, especially sensory ones. Synthetic, recombinant NGF is a proposed therapy for HIV- and drug-associated neuropathies.

Neural: Relating to a nerve or nerves.

Neuralgia: A sharp, shooting pain along a nerve pathway.

Neurology: The branch of medical science concerned with the nervous system (including the brain) and its disorders.

Neuropathy: An illness involving the nerves. Nerves are responsible for (among other things) the movement of muscles and the sensation of touch, including the sensation of pain. The symptoms of a neuropathy can therefore be weakness of a muscle or pain and tingling. In people with HIV infection, the most frequent symptoms of neuropathy are painful feet and legs.

Neuropsychological Defects: Alterations in behavior that are related to a central nervous system illness and interfere with an individual's ability to function in an age-appropriate fashion.

Neuropsychological Test: One of several tests designed to measure certain aspects of brain function, such as memory, concentration, attention and visual/motor skills.

Neurosyphilis: A form of advanced syphilis in which the infection has spread to the central nervous system.

Neutralizing Antibody: An antibody that neutralizes (renders harmless) the infectivity of microorganisms, particularly viruses.

Neutropenia: Abnormal drop in the number of a type of white cells called neutrophils.

Neutrophilia: Abnormal rise in the number of a type of white blood cells called neutrophils.

Neutrophil: The most common type of white blood cell. Neutrophils release chemicals involved in inflammation, and are the immune system's primary defense against bacterial infections. The normal range for neutrophils is from 3,000 to 7,000.

Nevirapine: A non-nucleoside reverse transcriptase inhibitor (see NNRTI) that has shown antiviral activity in people with AIDS, although resistance is quick to develop. Possible side effects include severe rash, fever and liver impairment.

NF-KB (NF-KAPPA B): A regulatory protein that binds to certain genes which code for IL-2. HIV and increases their activity.

NIAID: National Institute of Allergy and Infectious Diseases. One of the institutes of the National Institutes of Health (NIH) which is part of the Public Health Service of the federal government. The NIAID is responsible for the federally funded national AIDS research program.

NK Cell: See Natural Killer Cell.

NNRTI (Non-Nucleoside Reverse Transcriptase Inhibitor): A member of a class of compounds, including delavirdine, loviride and neviripine, that acts to directly combine with and block the action oh HIV's reverse transcriptase. In contrast, nucleoside analogs block reverse transcriptase by capping the unfinished DNA chain that the enzyme is construction. NNRTIs have suffered from HIV's ability to rapidly mutate and become resistant to their effects.

Nodule: A rounded lump, knot or swelling of the skin.

Non-Directive Counseling: Describes a type of counseling in which the counselor supplies information and helps the client to arrive at a decision that reflects the client's needs and wishes.

Non-Hodgkin's Lymphoma (NHL): An AIDS defining illness which is a lymphoma made up of B-cells and characterized by nodular or diffuse tumors that may appear in the stomach, liver, brain and bone marrow of people with HIV. After Kaposi's sarcoma, NHL is the most common opportunistic cancer in people with AIDS.

Nonoxynol-9: A spermicide. In large enough concentration, has anti-HIV effects.

Nucleoside: A building block of DNA or RNA, the genetic material found in living organisms. Before being added to a DNA or RNA sequence, nucleosides must have a phosphate group added. See Phosphorylation.

Nucleoside Analog: A type of antiviral drug, such as AZT, ddI, ddC, or D4T, whose makeup constitutes a defective version of a natural nucleoside. Nucleoside analogs may take the place of the natural nucleosides, blocking the completion of a viral DNA chain during infection of a new cell by HIV. The HIV enzyme reverse transcriptase is more likely to incorporate nucleoside analogs into the DNA it is construction than is the DNA polymerase normally used for DNA creation in cell nuclei.

Nucleotide: A phosphorylated nucleoside.

Nystatin: An antifungal drug used primarily as a topical agent for oral candidiasis.

Ocular: Relating to the eye.

Off-Label: Use of a drug for a disease or condition other than the indication for which it was approved by the FDA. For example, many doctors prescribe paromycin (humatin) for cryptosporidiosis, although it is not approved for treating this disease.

Oncology: Study of cancer and/or tumors.

Open-Label Trial: A study in which both researchers and participants know what drug a person is taking and at what dose.

Opiate: A natural or synthetic derivative of opium that has similar analgesic and sedative effects.

Opportunistic Infections (OI): Infections that occur in persons with weak immune systems due to AIDS, cancer or immunosuppressive drugs such as corticosteroids or chemotherapy. Toxoplasmosis, PCP, and cytomegalovirus are all examples of OIs.

Opportunistic Tumors: Opportunistic tumors, like opportunistic infections, occur primarily in people with weakened immune systems, precisely because the immune system is weak. In people with HIV infection, the major opportunistic tumors are Kaposi's sarcoma and certain types of lymphoma.

Opthalmological: Relating to the medical specialty of the eye.

Optimal Health: The highest state of well-being attainable by a person at a particular time in his or her life. Although the optimal health for an HIV-infected person may be different from that of someone who is HIV-negative, optimal health should still be the goal for care of an HIV-infected individual.

Oral Candidiasis: Also known as thrush; an infection in the mouth caused by the yeast-like fungus Candida albicans. It often is one of the first symptoms of a weakened immune system in HIV positive individuals. In the mouth, oral candidiasis appears as white or red patches.

Oral Hairy Leukoplakia (OHL): It is caused by the same virus (EBV) that causes one type of infectious mononucleosis. The symptoms of oral hairy leukoplakia are white (leuko) patches (plakia) with a ribbed or "hairy" surface that appear on the side of the tongue and inside cheeks. It usually produces no symptoms, but may distort taste or cause pain. These patches often appear similar to those of thrush; in fact, oral hairy leukoplakia is often diagnosed when people who appear to have thrush do not respond to the usual treatment. It can also be diagnosed with a biopsy of the patches. Oral hairy leukoplakia seems to occur exclusively in people with HIV infection. It generally indicates progressive weakening of the immune system. The treatment for oral hairy leukoplakia is an antiviral drug called Acyclovir.

Organelle: One of the specialized parts of a living cell.

Organic Molecule: A molecule with a basic skeleton made up of a skeleton of carbon atoms plus hydrogen and oxygen atoms and, in proteins, nitrogen. Organic molecules may also include isolated atoms of other elements.

Orphan Drug: A status granted by the FDA to unpatentable medications developed for rare diseases. Orphan drug status gives the drug's manufacturer a seven-year right to exclusively market the compound. This protection of unpatentable orphan drugs encourages their development by greatly increasing their profitability.

Oxidation: A chemical reaction resulting from exposure to oxygen or other electron-donating atom or molecular combination of atoms. On the cellular level, oxidative reactions are the source of energy, but free radicals and other oxidizing agents can damage cellular components such as membranes and interfere with cell's regulatory systems.

Oxidative Stress: Physiological effects of increased levels of free radicals and oxidating molecules associated with disease and aging; effects include cell membrane damage and cell death. This is a highly oxidized environment within cells that is thought to promote HIV replication because cells are forced into a highly activated state due to loss of control of their regulatory systems.

p24: One of the several proteins (the protein with a molecular weight of 24,000) that make up HIV (specifically the core). It can be measured in blood and other body fluids.

p24 Antigen Test: Although less accurate, the p24 antigen test is, like the PCR test (see Polymerase chain reaction) and a culture for HIV, a test that detects the presence of HIV in the blood. The test has been used to monitor viral activity. An antigen is anything that causes the immune system to identify it as foreign and to manufacture antibodies against it. A p24 antigen test detects p24 and therefore HIV. Unlike PCR and HIV cultures, however, the p24 antigen test is not especially sensitive, and most people with HIV infection have tests for the p24 antigen that are negative. Levels of p24 are highest both early and late in the disease; the numbers of HIV are likewise highest at the same times.

Package Insert: A form containing the indications, side effects and other relevant information known about a drug that can be found on the inside of any prescription drug container.

Palliative: Offering comfort or relief of symptoms without making the underlying disease process any less or better. It is the type of care offered in a hospice.

Pancreatic Enzyme: One of the proteins made by the pancreas that aids digestion of fats, carbohydrates and proteins.

Pancreatitis: Inflammation of the pancreas; symptoms may include intense abdominal pain, nausea, vomiting, constipation and possibly jaundice; pancreatitis can be life-threatening. Its onset may be predicted by rises in blood levels of the pancreatic enzyme amylase. The anti-HIV drugs ddI and more rarely, ddC may cause pancreatitis in some individuals.

Pandemic: Denoting a disease affecting the population of an extensive region of the world, e.g., HIV disease.

Papanicolaou (Pap) Smear: A microscopic examination of the surface cells of a woman's cervix, usually conducted on scrapings from the opening of the cervix. This assay test is used to detect changes in cervical cells that could be forerunners of cancer.

Papillomavirus: The virus group that includes the cause of genital warts or condylomata.

Papule: A small raised bump of any color (but often red) on the skin. Papules can occur individually or in clusters.

Parallel Track Program: A system of distributing certain experimental drugs to individuals who are unable to participate in ongoing clinical trials of that drug.

Parenteral: Intravenous or intramuscular administration of substances such as therapeutic drugs or nutritive solutions.

Parenterally: Infusion by injection.

Paresthesia: Abnormal sensations such as burning or tingling. Paresthesia may constitute the first symptoms of peripheral neuropathy, or it may be a limited drug side effect that does not worsen over time.

Paromomycin (Humatin): An antibiotic in pill form used for the treatment of intestinal infections, cryptosporidiosis in particular. Possible side effects include stomach upset and diarrhea.

Paronychia: Inflammation of the tissue surrounding the fingernail; may be due to infection by bacteria or fungi.

Parotitis: Inflammation of the parotid gland caused by viral or bacterial infection.

Partner Notification: The process of informing sexual or needle-sharing partners of an HIV-infected person that they have been or are at risk of contracting HIV infection. May be done by the HIV-infected person, health care provider, or a public health worker.

Passive Immunotherapy: A process in which individuals with advanced disease (who have low levels of HIV antibody production) are infused with plasma rich in HIV antibodies or an immunoglobulin concentrate (HIVIG) from such plasma. The plasma is obtained from asymptomatic HIV-positive individuals with high levels of HIV antibodies.

Pastille: A medicated disc or tablet dissolved in the mouth.

Pathogen: An organism or material capable of causing disease.

Pathogenesis: Description of the development of a particular disease, especially the events, reactions and mechanisms involved at the cellular level.

PCP (Pneumocystis Carinii Pneumonia): A pneumonia caused by an infection with Pneumocystis carinii (which is either a protozoa or fungus - it has characteristics of both). Pneumocystis Carinii is common in the lungs, however, in people with weakened immune systems it grows rapidly and is the most frequent serious opportunistic infection in people with HIV infection. When there is no explanation for immune suppression other than HIV infection, pneumocystis is an AIDS-defining diagnosis. The symptoms are cough without sputum, shortness of breath, and fever. These symptoms usually evolve over a period of several days or, more commonly, weeks. The diagnosis is generally established by a chest x-ray or studies of lung function, combined with a microscopic examination of respiratory secretions. Treatment is most successful when started relatively early in the course of the infection. Bactrim is the most effective prophylaxis for PCP. Pneumocystis Carinii infection sometimes may occur elsewhere in the body (skin, eye, spleen, liver or heart).

PCR (Polymerase Chain Reaction): A highly sensitive test that measures the presence or amount of RNA or DNA of a specific organism or virus (for example, HIV or CMV) in the blood or tissue. Unlike the standard blood test for HIV infection which detects antibodies to HIV, the PCR detects HIV itself. PCR tests are being used to gauge HIV disease progression and the effect of particular treatments on HIV infection.

Pentamidine (Pentam, NebuPent): An antibiotic used in aerosol form as a prevention against PCP ("aerosolized pentamidine") and used intravenously to treat PCP. When given by vein, pentamidine often has such side effects as low blood pressure (causing fainting), low blood sugar, high blood sugar (diabetes), pancreatitis and kidney disease. Side effects of inhaled pentamidine can include coughing, lung contractions, shortness of breath and fatigue.

Pelvic Inflammatory Disease (PID): A gynecological condition caused by an infection (usually sexually transmitted) that spreads from the vagina to the upper parts of a woman's reproductive tract in the pelvic cavity. PID takes different courses in different women, but can cause abscesses and constant pain almost anywhere in the genital tract. If left untreated, it can cause infertility or more frequent periods. Severe cases may even spread to the liver and kidneys causing dangerous internal bleeding, lung failure and death. PID can be more difficult to treat or recur in HIV-positive women. Early treatment is usually with oral antibiotics, some cases require intravenous treatment.

Pentoxifylline (Trental): A drug that reduces levels of tumor necrosis factor (TNF) Pentoxifylline is FDA approved for treatment of leg cramps and poor circulation. Possible side effects include nausea and other digestive upset, dizziness and headache.

Peptide: two or more chemically linked amino acids.

Perinatal Transmission: Transmission of a pathogen, such as HIV, from mother to infant by blood

or body fluids. May occur in utero, at the time of delivery, and possibly by breast-feeding.

Peripheral Neuropathy: A condition characterized by sensory loss, pain, muscle weakness and wasting of muscle in the hands or legs and feet. It may start with burning or tingling sensations or numbness in the toes or fingers. In severe cases, paralysis may result. Peripheral neuropathy may arise from an HIV-related condition or be the side effect of certain drugs, some of the nucleoside analogs in particular.

Peripheral: The surrounding area. As an example, peripheral neuropathy involves the area surrounding damaged nerves.

Peripherally Inserted Central Catheter: See PICC line.

Peyer's Patch: One of the lymphatic nodules aggregates existing in the intestines.

Persistent Generalized Lymphadenopathy (PGL): A diagnosis of PGL means that lymph glands are swollen for at least one month and at two different sites of the body, not counting the groin area. PGL often occurs early in HIV infection and is generally of little consequence unless the symptoms have actually been caused by another disease. (See Lymph glands and Lymphadenopathy.)

Phagocytosis: The process by which white blood cells such as macrophages engulf and destroy foreign material, dead tissues and cells.

Pharmacokinetics: The extent the body is able to absorb, distribute and eliminate a drug over time.

Phase I Clinical Trial: The earliest stage clinical trial for studying an experimental drug in humans. Phase I trials are generally comparatively small, typically involving 20 to 100 patients and lasting several months. They provide an initial evaluation of a drug's safety and pharmacokinetics - how the drug is absorbed, what tissues it reaches and how long it takes to leave the body. Such studies also usually test various doses of the drug (dose-ranging) to obtain an indication of the appropriate dose to use in later studies. Approximately 70 percent of drugs successfully complete phase I.

Phase II Clinical Trial: A more advanced stage clinical trial that follows the Phase I trials. A phase II trial gathers preliminary information on whether an experimental drug works. The major purposes are to continue to determine short-term safety and, primarily, effectiveness. Data are often based on laboratory tests that provide quick, but indirect measurements of a drug's effect on disease (see surrogate marker). Phase II trials often involve up to several hundred people who are randomly assigned to take either the experimental drug or a "control" (the standard treatment for the disease or no treatment at all. Usually the trial is double-blinded, which means no one (not the patient, doctor, nurse or researcher) knows who is getting the drug until the trial is completed and the results are analyzed. Approximately 33 percent of drugs successfully complete phase II.

Phase III Clinical Trial: An advanced stage clinical trial that should conclusively show how well a drug works as compared to other treatments. Typically involves from several hundred to several thousand patients, take place at multiple sites, and may last from 1 to 4 years. They should measure whether a new drug extends survival or otherwise improves the health of patients on treatment (clinical improvement) rather than just provide surrogate marker data. Approximately 25 to 30 percent of drugs successfully complete phase III.

Phosphorylation: The addition of a phosphate group (phosphate plus four oxygen atoms) to an organic molecule.

Photosensitivity: Heightened skin response to sunlight or ultraviolet light (rapid burning when exposed to the sun).

PICC Line (Peripherally Inserted Central Catheter): A catheter inserted into an arm vein and used for periods of up to three months. This catheter does not need to be surgically implanted and can be inserted at home by a trained nurse.

Placebo: A "dummy pill," "sugar pill," or look alike material containing no medicine, may also be the standard treatment. Used to compare against effects of experimental drugs. In placebo-controlled trials, the control group takes the placebo, while the test group takes an experimental drug. Many such studies are also double-blinded, which means that neither doctors nor patients know who is receiving drug or placebo.

Placebo effect: Improvements in health experienced or perceived by people who are taking a placebo.

Placebo-controlled study: A method of investigation of drugs in which an inactive substance or the standard therapy (the placebo) is given to one group of patients while the drug being tested is given to another group. The results obtained in the 2 groups are then compared.

Placenta: The vascular organ uniting fetus and (maternal) uterus, through which metabolic exchange occurs between fetus and mother.

Plasma: A fluid that carries blood cells and nutritive substances throughout the body. Plasma also removes metabolic waste products from body organs and is a medium for chemical communications between different parts of the body.

Platelets: Small, specialized cell fragments in blood that trigger the clotting of blood so that damaged vessels stop bleeding. Normally 150,000 to 300,000 platelets are found in one cubic centimeter of blood, but platelet counts can become sharply depleted in people with HIV infection, sometimes so extremely low that the person is prone to bleeding. See Immune Thrombocytopenia Purpura. The cause of the low platelets may be HIV infection itself, or it may be the drugs that are used to treat people with HIV infection. Another function of platelets is to collect antigen-antibody complexes in the blood. Platelets coated with such complexes are eliminated from the body. The source of platelets is megakaryocyte cells in the bone marrow.

PML (Progressive Multifocal Leukoencephalopathy): A rapidly debilitating opportunistic infection that is found only in people with severely weakened immune systems, including people with HIV infection. Caused by the "JC" virus which infects brain tissue and causes damage to the brain and the spinal cord. PML has a distinctive appearance on CAT or MRI scans of the brain, but a diagnosis can be established definitely only with a biopsy. The infection tends to be progressive, and there is no standard treatment, although some doctors are experiencing success treating PML. Symptoms vary from patient to patient but include loss of muscle control, paralysis, blindness, problems with speech and an altered mental state.

Pneumocystis Carinii Pneumonia: See PCP.

Pneumococcal Vaccine: Pneumococcal vaccine is recommended for people, including people with HIV infection, who are especially prone to frequent or severe infections. Pneumococcus is caused by a bacterium called Streptococcus pneumonia or pneumococcus and is a common cause of bacterial pneumonia in people with HIV. It is best to take this vaccine relatively early in the course of the disease when the immune system is strong.

Pneumonia: Pneumonia is an infection of the lungs. The usual symptoms are cough, fever, and shortness of breath. The causes of pneumonia vary, and the treatment depends on the cause.

Podophyllin: Acidic resin from the May Apple plant that is painted on warts to remove them.

Polymerase Chain Reaction: See PCR.

Polyneuropathy: A disease process involving a number of peripheral nerves.

Polyphenol: An antioxidant contained in tea and red wine.

PPD (Purified Protein Derivative) Test: A simple skin test used to detect prior exposure to tuberculosis. PPD is injected just under the skin of the forearm. After 48 to 72 hours, if the injection site will exhibit a red, hard bump if a person has been infected with TB and is not anergic.

Pre-Clinical: Refers to the testing of experimental drugs in test tubes or in animals - the testing that occurs before trials in humans may be carried out.

Pregnancy Counseling: Process of discussing with a woman of childbearing age her options regarding whether to become pregnant or, if she is already pregnant, her options regarding continuing or terminating the pregnancy.

Primary Care Provider: A health care provider (e.g., physician, physician assistant, nurse practitioner) who offers and coordinates comprehensive patient care.

Primary Care Setting: A place where comprehensive care is delivered (e.g., a physician's office, community health clinic, preventive nursing service).

Primary Infection: The initial introduction of an infection, such as HIV or CMV, into a person. Primary HIV infection (also called acute HIV infection) is sometimes characterized by a flu-like illness with fever, malaise, enlarged lymph glands and sometimes a sore throat or rash. This initial infection precedes seroconversion.

Principal Investigator: The head researcher responsible for organizing and overseeing a clinical trial.

Procrit: See Epogen

Prodrug: A compound that is converted within the body into its active form that has medical effects. Prodrugs are useful when the active drug may be too toxic to administer systemically, the active drug is absorbed poorly by the digestive tract, or the body breaks down the active drug before it reached its target.

Progesterone: A female hormone whose function is to prepare the uterus for the reception and development of the fertilized ovum (egg).

Prognosis: The probable future course of disease in a patient.

Prophylaxis: Treatment to prevent the onset of a particular disease ("primary" prophylaxis) or the recurrence of symptoms in an existing infection that has been brought under control ("secondary" prophylaxis or maintenance therapy).

Protease (Proteinase): An enzyme that triggers the breakdown of proteins. HIV's protease enzyme breaks apart long strands of viral protein into the separate proteins making up the viral core. The enzyme acts as new virus particles are budding off a cell membrane.

Protease Inhibitors: A drug that binds to and blocks HIV protease from working, thus preventing the production of new infectious viral particles. Many different protease inhibitors are currently in clinical trials.

Protein: Large molecules made up of long sequences of amino acids that are formed naturally by plants and all living organisms. Some hormones, enzymes and cellular structures are proteins. A n essential human nutrient, proteins provide the structures necessary for the growth and repair of living cells and tissue.

Protocol: A detailed plan that describes the details of a clinical trial, its rationale, goal, the drugs involved, their dosage levels, treatment duration and who and how many may participate.

Protozoa: A large group of one celled (unicellular) animals, including amoebas. Some protozoa cause parasitic diseases in people with AIDS, notable toxoplasmosis and cryptosporidiosis.

Prozone Phenomenon: A reaction that occurs in undiluted or slightly diluted serum in which antibody is present in such high concentration that it interferes with precipitation reactions with antigens. The phenomenon may interfere with obtaining a correct result from a test especially a test for syphilis.

Pruritus: The symptom of itching. It may come and go or be constant and may be associated with skin lesions or occur independent of any skin lesion.

Pruritic: Itchy.

Psoriasis: A condition characterized by the eruption of circumscribed, discreet and confluent, reddish, silvery-scaled bumps or lesions predominantly on the elbows, knees, scalp, and trunk.

Psychomotor: Relating to mental functioning and muscular movement.

Pulmonary: Referring to or relating to the lungs.

Purified Protein Derivative: Protein-rich material derived from the microorganism M. tuberculosis and used as a skin-test reagent to detect current or prior infection with that organism. See PPD.

PWA: PWA is the abbreviation for people with AIDS.

Pyrazinamide: An antibiotic used as part of multidrug combinations to treat tuberculosis.

Pyrimethamine (Daraprim): Pyrimethamine is an oral antiprotozoa drug used in combination with a sulfa drug like sulfadiazine or clindamycin to treat toxoplasmosis. Pyrimethamine is taken by mouth. Its many possible side effect include severe allergic reactions and rashes, anemia, leukopenia, thrombocytopenia, insomnia and diarrhea. To avoid anemia, another drug, leucovorin, is given at the same time.

Quality Of Life: Expression used in speaking of issues relating to normalizing the life of a chronically ill individual. In defining quality of life, health care providers must consider not only the physical responses to medical therapy, but also the psychological implications of illness for both the patient and family. The overriding goal of care should be to relieve suffering and increase patient well-being.

Quinones: An antioxidant that is part of a family of ring-shaped organic molecules.

Radiation: That which gives off energy, waves or rays. It may be a substance which is used to diagnose or treat symptoms.

Radical: A group of elements or atoms usually passing intact from one compound to another, but usually incapable of prolonged existence in a free state.

Randomization: The process by which patients in a clinical trial are randomly assigned to different treatments. Randomization minimizes the differences among groups by equally distributing people with particular characteristics among all the trial arms.

Randomized Trial: A trial in which the participants are randomly assigned to receive one of the treatments under study or a placebo. See randomization.

Rapid Plasma Reagin (RPR): A nontreponemal test for detection of syphilis, the basis of which is agglutination.

Receptor: The specific protein-binding site in the membrane of the target cell or within its interior. Crucial for intercellular communication, receptors must combine with chemical messengers in order for them to exert their effects.

Recombinant: Refers to compounds produced by laboratory or industrial cultures of genetically engineered living cells. The cell's genes have been altered to give them the capability of producing large quantities of the desired compound for use as a medical treatment. Recombinant compounds often are versions of naturally occurring substances.

Rectum: The terminus (end) of the large intestine, including the anus.

Refractory: Severe disease that is resistant to treatment.

Relapse: Return of a disease after recovery.

Remission: A period when the signs of a disease have been eliminated through treatment or the immune response. A disease may be in remission without a complete cure having been effected.

Renal: Of or relating to the kidneys.

Replicate: To duplicate or reproduce.

Resistance (to a drug): The ability of an organism, a microorganism or a virus to lose its sensitivity to a drug. For example, after long term use of AZT, HIV can develop strains of virus in the body that are no longer suppressed by the drug, and therefore are said to be resistant to AZT. Resistance is thought to result from a genetic mutation. In HIV, such mutations can change the structure of viral enzymes and proteins so that an antiviral drug can no longer bind with them as well as it used to. Resistance detected by searching a pathogen's genetic makeup for mutations thought to confer lower susceptibility is called *genotypic resistance*. Resistance found by successfully growing laboratory cultures of the pathogen in the presence of a drug is called *phenotypic resistance*. High-level resistance reduces a drug's virus-suppressing activity hundreds of times. Low-level resistance represents only a few fold reduction in drug effectiveness. Depending on the toxicity of the drug, low-level resistance may be overcome by using higher doses of the drug in question.

Retina: The multilayered, light-sensitive membrane lining the inner eyeball that sends visual images to the brain via the optic nerve.

Retinal Depigmentation: Loss of the color in the back part of the eye.

Retinal Detachment: A condition in which a portion of the retina becomes separated from the inner wall of the eye. Retinal detachment can result from retinal disease such as CMV retinitis. The condition can rapidly lead to vision loss, but is treatable by adding silicone to the eye's vitreous humor to increase the pressure on the retina.

Retinitis: An inflammation (itis) of the retina, the layer of cells at the back of the eye that collects and send images to the brain. Retinitis usually causes some loss of vision. In people with HIV infection, the most common cause of retinitis is infection with cytomegalovirus. If left untreated it can lead to blindness.

Retrovirus: A type of virus that does not have double-stranded DNA, the molecule that holds the code which cells use to reproduce themselves. Instead, retroviruses have single stranded RNA, a molecule that holds the retrovirus's code, and an enzyme called reverse transcriptase, that turns RNA into DNA. When a retrovirus invades one of the cells of the body, it uses reverse transcriptase to turn its own RNA into DNA. This DNA then becomes part of the cell's DNA, which in turn produces the retrovirus instead of the cell. Many different kinds of retroviruses infect many different kinds of animals. HIV is the most important retrovirus to infect humans; it causes disease in no other animal species.

Rev: A regulatory protein produced by HIV within infected cells. Rev helps transport HIV RNA sequences (messenger RNA) out from the nucleus into the cell's cytoplasm, where it directs construction of proteins for new virus particles.

Reverse Transcriptase (RT): A viral enzyme that transcribes viral RNA into DNA so that genetic material of the virus can be integrated into genetic material of the T-cell helper and other host cells. Many antivirals inhibit the action of this enzyme, including AZT, ddI, and ddC.

Ribavarin: A nucleoside analog approved as a treatment for respiratory syncytial virus. Ribavarin has also shown activity against hepatitis C, but its use in HIV infection is highly controversial. It is possible

that it enhances the activity of ddI.

Rifabutin (Mycobutin): An oral drug FDA-approved as a preventative treatment for Mycobacterium avium complex (MAC) in people with AIDS and CD4 counts of less than 75. Rifabutin is also used in combination with other drugs for the treatment of active MAC infection. Possible side effects include neutropenia, eye and muscle irritation and a brown-orange discoloration of skin and urine.

Ribozyme: A recombinant RNA/enzyme combination designed to fit onto and cleave specific viral or cancerous genetic sequences from a cell's DNA. The gene for an anti-HIV ribozyme may be inserted into a cell to protect it from the virus' activity.

Risk Factor: A condition or behavior that makes it likely that a person with the risk factor will develop a condition. The major risk factors for HIV infection are needle-sharing with intravenous drug users and unprotected sexual contact with a person who has or may have been exposed to HIV. Another risk factor is having received blood products between 1978 when HIV infection was first known to exist in the United States and May 1985, when the blood supply was first screened for HIV. Another risk factor is sexual contact without barrier protection. Still another is to be born to a woman with HIV infection: approximately 25 to 30 percent of women who are infected with HIV will pass the virus to the unborn infant. A minor risk factor is needlestick injuries in health care workers who care for people with HIV infection. Less than one percent of all people with HIV infection in the United States have no clearly defined risk factor, although many of these people either are too sick to provide adequate information or are providing information that is suspect.

Risk Reduction: Process by which an individual changes behavior so as to decrease the likelihood of acquiring an infection.

Ritonavir (ABT-538): A protease inhibitor under development by Abbot Laboratories. It has produced drops in HIV viral load of greater than 99 percent in some people.

RNA (Ribonucleic acid): A single-stranded nucleic acid resulting from the transcription of genetic information in DNA. Controls the synthesis of protein in all living cells and can take the place of DNA in some viruses, including HIV.

Ryan White CARE (Comprehensive AIDS Resources Emergency) Act: Passed in 1990 to provide services for persons with HIV infection, this act seeks "to improve the quality and availability of care for individuals and families with HIV disease." It directs financial assistance to metropolitan areas with the largest numbers of reported cases of AIDS for emergency services and to all States for improved care and support services and early intervention services.

Safer Sex: Safer sex is a qualitative term. To be absolutely safe, sexual contact cannot involve an exchange of any bodily fluids— specifically, blood, semen or vaginal secretions. The term safer sex recognizes the likelihood of human error and the inexactness of human knowledge. Safer sex refers to sexual practices using a barrier (condom and spermicide, dental dam), or sexual practices that do no involve exchange of bodily fluids.

Salmonella: A bacterium sometimes found in raw meat, poultry or eggs that can cause severe diarrhea and even death, if untreated. There are many types of salmonella.

Salmonella Septicemia: An AIDS defining opportunistic infection. It is a form of food poisoning caused by the bacteria Salmonella which causes abdominal pain, fever and diarrhea. It is diagnosed by blood or stool culture.

Salmonellosis: Food poisoning caused by the bacteria Salmonella which causes abdominal pain, fever and diarrhea.

Salvage Therapy: The final possible treatment for people who are nonresponsive to or cannot tolerate other available treatments for a particular treatment.

Sarcoma: Cancerous growth or tumor on the skin or soft tissue.

Saquinavir (Invirase): A protease inhibitor developed by Hoffman-LaRouche. Is available at pharmacies. However, the current formulation has poor bioavailability. May be more successful at higher doses.

Scabies: Contagious itch or rash caused by asitic mites.

Scavenger Cell: One of a diverse group of white blood cells with the capacity to engulf and destroy foreign material, dead tissues and cells. See also Phagocytosis.

Sclerotherapy: Sclerosing therapy; treatment that involves injecting a solution into vessels or tissues that will cause them to harden.

Scid mice: Scid mice are used in studies as models of humans with immune diseases such as AIDS.

Seborrhea: A common eruption or rash of the scalp, midline of the face and chest, which often has an underlying fungal component. It may be severe in individuals with advanced HIV disease.

Secondary Infection: Reinfection with any infectious organism, including bacteria and viruses.

Secondary Care Setting: A place where patients are referred for special care (e.g., a community or general hospital).

Seborrhea: Dry skin condition.

Seizure: Uncontrolled movements of the arms and legs accompanied by unconsciousness and inability to control urine or stool. The usual cause of seizures in people with HIV infection is an opportunistic infection or an opportunistic tumor of the brain, including toxoplasmic encephalitis, cryptococcal meningitis, or lymphoma. Less commonly, seizures are caused by an imbalance of electrolytes or by medications. Recurrent seizures can usually be controlled with drugs like Dilantin and phenobarbital. Anyone with recurrent seizures should be careful about his or her physical circumstances. In many states it is illegal for a person with seizures to drive until seizures have been controlled for at least one year.

Selenium: A metallic element whose biological role is linked to glutathione.

Sentinel Surveillance: Surveying the prevalence of HIV in a certain geographic area or population.

Sensitivity: The ability of a test to correctly identify an individual who is infected.

Septra: See TMP/SMX

Septicemia: A serious condition caused by large numbers of bacteria in the blood. This condition can be fatal. Symptoms are a sudden drop in blood pressure and changes in heart rate and temperature.

Sepsis: The presence of pathogenic (disease-causing) organisms or their toxins in the blood or tissues and the associated abnormal bodily responses. Septicemia is one form of sepsis. Sepsis is life-threatening.

Seroconversion: Development of detectable antibodies to a substance or organism, such as HIV in the blood serum as a result of infection. It may take several months or more after HIV transmission for antibodies to the virus to develop. After antibodies to HIV appear in the blood, a person will test positive in the standard ELISA test for HIV.

Serologic Test: Any of a number of tests that are performed on the clear, liquid portion of blood (serum). Often refers to a test that determines the presence of antibodies to antigens such as viruses.

Seronegative: Having a negative test for antibodies to a substance or organism, such as HIV.

Seropositive: Having a positive test for antibodies to a substance or organism, such as HIV.

Seroprevalence: For HIV, the rate at which a given population tests positive on the ELISA test for HIV antibodies. The seroprevalence rate is nearly the same as the rate of HIV infection in a given population, leaving out mainly those who were recently infected.

Seroreverter: Describes a person whose antibody status has changed from positive to negative. Used to describe perinatally exposed infants who are not truly infected and become HIV antibody negative as they lose maternal HIV antibody.

Serostatus: The condition of having or not having detectable antibodies to a microbe in the blood as a result of infection. One may either have a positive or negative serostatus.

Serum: The clear portion of the blood from which cellular components have been removed.

SGOT: See AST.

SGPT: See ALT.

Shigellosis: An infection of the intestines caused by the bacteria Shigetta which causes abdominal pain, diarrhea and fever.

Shingles: A skin condition caused by reactivation of a Varicella zoster virus (VZV) infection, usually acquired in childhood (when it appears as chicken pox). It consists of painful blisters on the skin that follow the path of individual nerves. The blister generally dry and scab, leaving minor scarring. Standard treatment is with famciclovir or acyclovir. See also Herpes Virus.

Significance: An analytical evaluation of the results of a comparative trial or survey. Data yielding

a difference in outcome depending on treatment or environmental factors are considered statistically significant if various mathematical procedures indicate there is less than a one in twenty (five percent) chance that the same results would occur through random accident. (In statistical terms this is expressed as $p<.05$ - or, the p-value is less than .05).

Simian Immunodeficiency Virus (SIV): A retrovirus found in monkeys that is closely related to HIV.

Sinusitis: The sinuses are air sacs next to the passageway from the nose. Sinusitis is an infection of the sinuses, usually as a result of a cold or an allergy. Sinusitis is common in everyone, and is especially common in people with HIV infection. The reason for this is obscure. Symptoms are pus drainage from the nose, headache, face pain, and fever. The usual treatment is with antibiotics taken by mouth, such as trimethoprim-sulfamethoxazole, amoxicillin, erythromycin cephalexin (or Keflex), ciprofloxacin (Cipro), or tetracycline. Some people do not respond to these drugs, and their sinuses need to be drained, a procedure done by a specialist called an otolaryngologist (ear, nose, and throat specialist).

Side Effect: Action or effect of a drug other than that desired. The term usually refers to undesired or negative effects (drug toxicity). Investigational drugs must be evaluated for both immediate and long term side effects.

Sign: An indication of a disease or disorder that is observed by the health care provider.

Spleen: A large lymphatic organ in the upper left of the abdominal cavity with several functions: 1) trapping of foreign matter in the blood, 2) destruction of degraded red blood cells and foreign matter by macrophages, 3) formation of new lymphocytes and antibody production, and 4) storage of excess red blood cells.

Specificity: The ability of a test to correctly identify an individual who is not infected.

Spinal Tap: Also called a lumbar puncture, it is a procedure for obtaining cerebrospinal fluid, the fluid that surrounds the brain and the spinal cord. The procedure involves inserting a needle into the spinal cord. The cerebrospinal fluid is then analyzed for evidence of infection of the brain or spinal cord. Despite sounding unpleasant and risky, a spinal tap is a well-established medical procedure and is rarely associated with any important complications. The most common complaint is a severe headache for days following the spinal tap, a complaint made less likely by lying flat once the spinal tap is completed.

Sputum: Mucus or other matter that collects in the respiratory and upper digestive passages and is expelled by coughing or spitting.

Sputum Analysis: A method of detecting certain infections (especially tuberculosis) by culturing of sputum.

Squamous Intraepithelial Lesion (SIL): Findings in cells revealed by Pap smear that indicate cell changes requiring further evaluation.

Standard Therapy: A therapy that is FDA approved and widely used as first-line treatment.

Staphylococcus: A type of bacteria that may cause various types of infections.

Stavudine: See d4T.

STD: Sexually transmitted disease.

Stem Cell: Cell from which all blood cells derive. Bone marrow is rich in stem cells. Clones of stem cells may become any one of the repertoire of immune cells depending upon what cytokines and hormones they are exposed to.

Steroid: A member of a large family of structurally similar lipid substances. Steroid molecules have a basic skeleton consisting of four interconnected carbon rings. Different classes of steroids have different functions. All the sex hormones are steroids. Anabolic steroids increase muscle mass. Anti-inflammatory steroids (or corticosteroids) can reduce swelling, pain and other manifestations of inflammation. Any of numerous components that include sterols, certain hormones, D vitamins and some carcinogenic substances . Steroid drugs are often used to reduce inflammation in the body.

Stomatitis: Any of numerous inflammatory diseases of the mouth having various causes (e.g., mechanical trauma, irritants, allergy, vitamin deficiency, infection).

Strain: Subtype of a particular organism, as in a strain of HIV.

Subcutaneous: Beneath the skin. A subcutaneous injection goes just beneath the skin, not into the deeper muscle tissue.

Sub acute: Denoting a disease of moderate duration or severity; between acute and chronic.

Sublingual: Under the tongue.

Substernal: Beneath the sternum, a plate of bone that forms part of the front central wall of the thorax, commonly called the "breastbone."

Sulfadiazine: A sulfa drug used in combination with pyrimethamine for treating toxoplasmosis. Possible side effects include bone marrow suppression.

Superoxide Dismutase: One of the major cellular antioxidant enzymes. It removes surplus peroxide, an oxidizing free radical. Superoxide dismutase comes in two forms, one containing zinc and the other containing manganese.

Superantigen: An antigen that triggers immune response from a very large number of cells.

Suppressor T-Cell (T8, CD8): A subset of T-cells that halt antibody production and other immune responses.

Surrogate Markers: A laboratory measurement of biological activity within the body that indirectly indicates the effect of treatment on disease state. CD4 cell counts and viral load are examples of surrogate markers in HIV infection.

Symptom: Any perceptible, subjective change in the body or its functions that indicates disease or phases of disease as reported by the patient. Should be distinguished from a sign.

Symptomatology: The collected symptoms of a particular disease.

Syndrome: A group of symptoms and diseases that together are characteristic of a specific condition.

Syphilis: Infection caused by T. pallidum that if left untreated, can cause chronic infection of multiple organ sites including the central nervous system. When untreated in pregnant women can result in a life-threatening congenital infection in the newborn.

Synergy: The interaction of two or more treatments such that their combined effect is greater than the sum of the individual effects observed when each treatment is administered alone.

Systemic: Concerning or affecting the body as a whole. A systemic therapy is one that the entire body is exposed to, rather than just the target tissues affected by disease.

Taxol (Paclitaxel): A chemotherapeutic drug used for the treatment of solid tumors. There have been some successes using Taxol to treat ovarian cancer, it is also an experimental treatment for Kaposi's sarcoma. It works by inhibiting cell division and has a long list of side effects, in particular bone marrow suppression (resulting in neutropenia).

T-Cells (T-Lymphocyte): White blood cells (lymphocytes) that maturein the thymus and participate in a variety of cell mediated immune reactions. Three fundamentally different types of T cells are recognized: helper, killer and suppressor. Each has many subdivisions. See also lymphocyte.

T-Cell Percentage: T-helper cell counts are often reported as the percentage of all lymphocytes. The T-helper cell percentage is a more consistent and reliable measure of the amount of T-helper cells than the absolute number. Normal T-helper cell counts are usually greater than 30% of all lymphocytes.

T4 Cell: See CD4 cell.

T-Helper Cell (T-Helper Lymphocyte): An important type of immune system white blood cell (also known as a CD4 or T4 cell) that helps the body fight off infection. T-helper cells release cytokines that coordinate the activity of a broad range of immune cells, including B cells, which produce antibodies. HIV invades these cells and weakens or destroys them. Physicians regularly monitor T-helper cell counts in HIV infected individuals as an indicator of the progression of HIV disease; severe immune suppression is correlated with T-helper cell counts below 200. See CD4 cell.

T-Helper Cell Count: The number of helper lymphocytes present in a cubic millimeter (MM3) of blood. A T-helper cell count serves as an indicator of the severity or progression of HIV disease. T-helper counts have also been used in U.S. AIDS drug studies as surrogate markers for disease progression.

Tagamet (Cimetidine): A drug directed against histamine (H2) receptors; useful in the treatment of ulcers.

Tat: An HIV protein that helps produce new complete HIV RNA genomes, and ultimately new virus, from the HIV DNA genetic template present in infected cells. Tat may also be involved in: 1) the reactivation of other latent viruses in people with AIDS, such as JC virus, the cause of PML, 2) the development of AIDS-related KS by stimulating the formation of new blood vessels, and 3) the triggering of anergy and apoptosis in CD4 cells.

Tat Inhibitor: A drug used to stop the function of the HIV regulatory protein tat.

Teratogenicity: The ability to cause defects in a developing fetus. This is distinct from mutagenicity, which causes genetic mutations in sperms, eggs or other cells. Teratogenicity is a potential side effect of many drugs, such as thalidomide.

Testosterone: A naturally occurring male hormone, produced in the testes. A major male sex hormone; essential for spermatogenesis and maintains growth and development of reproductive organs and secondary sex characteristics of males. When administered as a drug, it can cause gain in lean body mass, increased sex drive and energy and possible aggressive behavior. Low testosterone levels are common in HIV infection.

TH Naive: A T cell that is not yet directed to produce either a cell-mediated (TH-I) or humoral (TH-2) response.

TH1/TH2 Cells: Subsets of T-helper lymphocytes, involved in cell-mediated immune responses. TH1 cells secrete IL-I and gamma interferon, which enhance cell-mediated responses and inhibit both TH2 subset cell activity and the humoral immune response. TH2 cells, the other subset of T-helper cells, are also involved in cell-mediated immune responses. TH2 cell activity and secretions are thought to inhibit cell-mediated responses and to enhance the humoral response. TH2 cells secrete IL-4 and IL-10.

TH1 Response: An acquired immune response whose most prominent feature is high cytotoxic T-lymphocyte activity relative to the amount of antibody production. The Th1 response is promoted by CD4 "Th1" T-helper cells.

TH2 Response: An acquired immune response whose most prominent feature is high antibody production relative to the amount of cytotoxic T lymphocyte activity. The Th2 response is promoted by CD4 "Th2" T-helper cells.

Thalidomide: A drug that reduces levels of TNF. It is being studied as a treatment for wasting and other complications of HIV, as well as a number of other diseases where TNF levels are a problem. Potential side effects include sedation, constipation, peripheral neuropathy and severe birth defects in the infants born to women who take the drug during pregnancy.

3TC (Lamivudine): A nucleoside analog with anti-HIV and anti-hepatitis activity. Possible side effects include hair loss.

Thrombocyte: See Platelet.

Thrombocytopenia: A low count (penia) of thrombocytes (or platelets), cells in the blood which facilitate clotting. The usual count of thrombocytes is 150,000 to 300,000 per milliliter of blood. Lower counts of 80,000 to 120,000 per milliliter are common in people with HIV infection. When the count is very low, from 5,000 to 25,000 per milliliter, bleeding problems may occur. People with HIV infection have thrombocytopenia because their bodies produce antibodies against their own platelets. Some people have no symptoms but must still be careful to avoid cuts or anything that could cause bleeding. Other people have excessive nosebleeds, excessive bleeding from cuts, and red spots the size of pinheads that come from tiny hemorrhages into the skin. Treatment is with drugs-corticosteroids (see above), AZT, gamma globulin given intravenously, alpha interferon with a

spleenectomy, the surgical removal of the spleen.

Thrush: An infection of the mouth caused by the fungus Candida albicans. The symptoms are white patches along the gums, on the inside of the cheeks, or on the tongue. Thrush is extremely common in people with HIV infection, and is easily treated with nystatin, clotrimazole, ketoconazole, or fluconazole.

Thymic Hormone: One of the hormones produced by the thymus that are believed to play a role in the maturation of T-lymphocytes and overall modulation of the immune system. Versions of several of them are under study and anti-HIV therapies - thymopentin and thymosin-α_1 in particular.

Thymus: A lymphoid organ in the chest that is the site of lymphocyte formation and maturation as well as the secretion of thymic hormones. An important function of the thymus is to weed out lymphocytes that react to proteins produced by the body ("self-antigens"), thus preventing autoimmune disease. The thymus is a large organ during childhood, but shrinks during adolescence.

Tinea: A fungal infection of the hair, skin or nails, including ringworm, "athlete's foot" and groin infection or "jock itch."

Titer: A standard of strength, per volume of test solution.

TMP-SMX (Trimethoprim-Sulfamethoxazole -Bactrim, Septra, and others): A combination antibiotic drug which is the first-line drug for the prophylaxis and treatment of PCP. May also be effective against toxoplasmosis and bacterial infections. Possible side effects include skin rash (which on rare occasions spreads to other body surfaces and becomes life-threatening Steven-Johnson syndrome), digestive disturbances, bone marrow suppression and liver impairment.

Topical Solvents: A liquid substance having dissolving properties when placed on the skin and/or mucous membranes.

Topoisomerase: An enzyme that uncoils the tightly wound DNA in cells' nuclei so that cell division and replication can take place.

Topotecan: An experimental anticancer chemotherapy that inhibits topoisomerase I and blocks cell division. It is a possible therapy for HIV, having been found to inhibit the HIV long terminal repeat in the lab, and PML, an opportunistic infection of the brain.

Total Parenteral Nutrition: See TPN.

TNF (Tumor Necrosis Factor Alpha, TNFα): A cytokine produced by macrophages that helps activate T-cells. It may also stimulate HIV activity. TNF levels are very high in people with HIV, and the molecule is suspected to play a part in HIV-related wasting, neuropathy and dementia.

TPN (Total Parenteral Nutrition): A liquid food substitute infused directly into the blood and designed to meet a person's entire nutritional needs. TPN provides an alternate route in cases of severe gastrointestinal distress in which nutrient absorption is poor. It strengthens the body and relieves the digestive tract while therapy for the underlying condition progresses. TPN's high cost

precludes its use as a long-term therapy.

Toxicity: State of being poisonous or harmful. The harmful effects of a given drug that occur during therapy. The term is similar to side effect and adverse reaction.

Toxin: A harmful or poisonous agent.

Toxoplasmosis: Toxoplasmosis is an infection caused by the parasite Toxoplasma gondii. Toxoplasma gondii is found in cat excrement and in rare meat, both of which are the most common sources of infection. About 30 percent of all adults in the United States have Toxoplasma gondii in their bodies, but the majority are unaware of it. The parasite remains dormant and rarely causes disease unless the immune system is weakened. In people with HIV infection, the most common form of toxoplasmosis is an infection of the brain called toxoplasmic encephalitis.

Toxoplasma Gondii (t. gondii): The parasite that causes toxoplasmosis.

Trachea: The windpipe, the passage in the throat leading to the lungs.

Transfusion: Putting whole blood, platelets, or plasma into the bloodstream.

Transmission: Transfer.

Transactivate: When one gene produced causes a different gene to be transcribed as activated.

Transaminases: Enzymes (proteins) that transfer amino acids in the body to another type of acid.

Transcription: The first step in protein synthesis, formation of messenger RNA, which conveys specific genetic information

Treatment Investigational New Drug (IND): An FDA approved program to use an experimental drug that appears to be safe, and may be effective, in a defined group of patients with serious or life-threatening conditions, and who have no satisfactory alternatives. The purpose is to facilitate availability of promising new drugs as early in the drug development process as possible. See also Compassionate Use, Parallel Track and Expanded Access.

Treatment Vaccine: Designed to produce new or renewed therapeutic immune response in a person already infected.

Trichloroacetic Acid: A strong acid solution used to dissolve venereal and other warts.

Trichomonas: A family of parasitic protozoan flagellates that cause disease in various animals including humans.

Triglyceride: Combination of fatty acid and glycerol found in blood.

Trimetrexate (Neutrexin): An antibiotic approved as an alternative treatment for moderate to severe PCP. Trimetrexate causes severe bone marrow, liver, kidney and gastrointestinal toxicities. It must be administered with leucovorin (folinic acid) to lessen these adverse effects.

Troche: Solid tablet form of a medical compound that is placed in the mouth and allowed to dissolve slowly, releasing the therapeutic agent.

Treponema Palladum: The micro-organism that causes syphilis: sometimes referred to as a spirochete because of its shape.

Trimethoprim-Sulfamethoxazole (TMP-SMX): A first-line combination drug for PCP prophylaxis and treatment. Possible side effects include rash, pruritus, cytopenia, liver abnormalities and gastrointestinal upset.

T-Suppressor Cell (T-Suppressor Lymphocyte): A type of white blood cell that helps regulate the body's response to an infection; also called CD8 or T8 lymphocyte.

Tuberculosis (TB): An infection, usually in the lungs that is far more frequent in people with HIV infection than in the general population. The bacterium that causes TB can either be dormant (inactive TB) or active (active TB). In active TB, the usual symptoms are fever and cough. People with either active or inactive TB will have skin tests that are positive for TB. In people with HIV infection, the skin test is less reliable, especially in the later stages of HIV infection when the immune system is weakened. People with HIV infection and inactive TB should receive treatment with a drug called isoniazid to prevent active TB. People with HIV infection and active TB should receive a combination of isoniazid and rifampin. TB is transmitted in close quarters when a person with active TB coughs the microbe into the environment.

Tuberculin-Reactive: Refers to someone who tests positive on a PPD skin test.

Tuberculin Unit (TU): Term used to describe doses of purified protein derivative used in PPD tests for TB.

Tumor Necrosis Factor (TNF): See TNF.

Ulcer: A break in skin or mucous membrane with loss of surface tissue.

Ultraviolet (UV): Denoting electromagnetic rays beyond the violet end of the visible spectrum; includes tanning and sunburn of the skin and is associated with the development of skin cancer.

Vaccine: A vaccine is a drug, given by mouth or by an injection, that stimulates the immune system to form antibodies to some microbe. The polio vaccine, for instance, stimulates the immune system to form antibodies against the polio virus. These newly formed antibodies now protect the person against any subsequent exposure to that microbe. Some vaccines work better than others: with the polio vaccine, protection is nearly 100 percent; with the influenza vaccine, protection is about 70 percent. Vaccines for HIV infection are being tested in people with and without HIV infection.

Varicella-zoster virus (VZV): A virus in the herpes family that causes chicken pox during childhood and may reactivate later in life to cause herpes zoster (shingles) in individuals with immunosuppression.

Vascular: Relating to or containing blood vessels.

Vector: An agent that transfers a pathogen from one organism to another (e.g., an insect).

Venereal Disease Research Laboratories (VDRL) Test: A screening test for syphilis developed at the Venereal Disease Research Laboratories.

Verrusol: A solution made of salicylic acid, podophyllum resin and cantharidin (Spanish fly), used to dissolve and blister skin growths such as warts and Molluscum contagiosum.

Vertical Transmission: Transmission of a pathogen such as HIV from mother to fetus in utero or during birth.

Viral Load or Burden: The number of viral particles (usually HIV) in a sample of blood plasma. HIV viral load is increasingly used as a surrogate marker for disease progression. It is measured by PCR and bDNA tests and is expressed in number of HIV copies or equivalents per milliliter.

Viremia: The presence of virus in the blood or blood plasma. Plasma viremia is a quantitative measurement of HIV levels similar to viral load but is accomplished by seeing how much of a patients plasma is required to start an HIV infection in a laboratory cell culture.

Virion: The complete viral particle.

Virology: The study of viruses and disease caused by viruses.

Virus: A virus is a tiny microbe that, unlike bacteria, can neither survive nor reproduce unless it lives in a cell. A virus is a noncellular entity, much smaller than bacteria, that is composed merely of genetic material (DNA or RNA) surrounded by a protein envelope. Viral genes subvert an infected cell's normal chemical processes to create new virus particles, usually killing the cell in the process. HIV is a virus that lives in CD4 lymphocytes in humans.

Vitamin: Organic molecules essential in small amounts for normal metabolism, growth and development of the body. See also micronutrient.

Vitreous Humor: A gel-like substance that fills the eyeball between and the retina.

Wasting Syndrome: A condition characterized by loss of ten percent of normal weight without obvious cause. The weight loss is largely the result of depletion of the protein in lean body mass and represents a metabolic problem frequent during AIDS. The causes of wasting vary; they may include opportunistic infections and tumors, or they may simply be the result of HIV infection itself. In some cases, wasting is accompanied by diarrhea; the condition is then called the diarrhea-wasting syndrome. Wasting can be an AIDS-defining diagnosis: according to the criteria of the Centers for Disease Control and Prevention.

Western Blot: A test for specific antibodies, in this case, for antibodies to HIV. (See ELISA.) The Western blot test, combined with an ELISA, is over 99 per cent accurate in both sensitivity and specificity. The combination of tests is generally offered free of charge from most health departments and at a cost of $20 to $150 from commercial laboratories. The ELISA is easily performed, but the Western blot is more complicated and often done only by reference laboratories or on certain days of the week. For this reason, the results may not be available for several days or even weeks. The test results are usually either positive or negative, but occasionally people have Western blots that can not be clearly interpreted and the test results are considered indeterminant. The usual recommendation for people with indeterminant results is

to have the test repeated in two or three months. People at a low risk for HIV and with indeterminant results almost never have HIV infection, and the cause of the indeterminant results is not known.

White Blood Cell: See Leukocyte.

X-Ray: A picture made by projecting roentgen rays through a body onto a photographic plate.

Yeast: A fungus which reproduces asexually and is dependent upon other organisms for food. Certain types of fungus like Candida albicans may cause disease through unrestrained growth.

Zalcitabine (ddC; trade name HIVID; also called dideoxycytidine): An FDA-approved nucleoside analog drugs that inhibits the reverse transcriptase enzyme of HIV. Its major limiting toxicity is peripheral neuropathy. It has the advantage of being 10 percent more potent than AZT and has been used in combination therapy with AZT in patients with advanced disease.

Zerit: Brand name for d4T (stavudine). See D4T.

Zidovudine: See AZT.

Zinc: A metallic element; a number of salts of zinc are used in medications.

Zidovudine: See azidothymidine (AZT).

Zinc: An essential mineral often depleted in persons with HIV. Zinc is a component of many enzymes. It is important in protecting cells against excess oxidation and helps immune cells mature and function. Ingesting high dosed of zinc can be harmful because it interferes with the absorption of copper, another essential micronutrient.

Zovirax: See Acyclovir.

Footnotes

Complied by Michael Cook and Lola Halpin, 1995.

Updated by Alicia A. Culver, February 1996.

APPENDIX A

"Georgia Living Will"

Living will made this _____ day of _____ (month, year)

I, _____, being of sound mind, willfully and voluntarily make known my desire that my life shall not be prolonged under the circumstances set forth below and do declare:

1. If at any time I should have a terminal condition as defined in and established in accordance with the procedures set forth in paragraph (10) of Code Section 31-32-2 of the Official Code of Georgia Annotated, I direct that the application of life-sustaining procedures to my body be withheld or withdrawn and that I be permitted to die;
2. In the absence of my ability to give directions regarding the use of such life-sustaining procedures, it is my intention that this living will shall be honored by my family and physician(s) as the final expression of my legal right to refuse medical or surgical treatment and accept the consequences from such refusal;
3. I understand that I may revoke this living will at any time;
4. I understand the full import of this living will, and I am at least 18 years of age and am emotionally and mentally competent to make this living will; and
5. If I am female and I have been diagnosed as pregnant, this living will shall have no force and effect during the course of my pregnancy.

Signed _____

_____ (City), _____ (County), and_____ (State of Residence).

I hereby witness this living will and attest that:

(1) The declarant is personally known to me and I believe the declarant to be at least 18 years of age and of sound mind;

(2) I am at least 18 years of age;

(3) To the best of my knowledge, at the time of the execution of this living will, I:

- (A) Am not related to the declarant by blood or marriage;
- (B) Would not be entitiled to any portion of the declarant's estate by any will or by operation of law under the rules of descent and distribution of this state;
- (C) Am not the attending physician of declarant or an employee of the attending physician or an employee of the hospital or skilled nursing facility in which declarant is a patient;
- (D) Am not directly financially responsible for the declarant's medical care; and
- (E) Have no present claim against any portion of the estate of the declarant;

(4) Declarant has signed this document in my presence as above instructed, on the date above first shown.

Witness _____ Witness _____

Address_____ Address_____

Additional witness required when living will is signed in a hospital or skilled nursing facility.

I hereby witness this living will and attest that I believe the declarant to be of sound mind and to have made this living will willingly and voluntarily.

Witness_____

(Medical director of skilled nursing facility, or staff physician not participating in the care of the patient, or chief of the hospital medical staff, or staff physician not participating in the care of the patient)

Paragraph (10), Code Section 31-32-2 of the Official Code of Georgia Annotated provides:

'Terminal condition" means incurable condition caused by disease, illness or injury which, regardless of the application of life-sustaining procedures, would produce death. The procedure for establishing a "terminal condition" is as follows: Two physicians who, after personally examining the declarant, shall certify in writing, based upon conditions found during the course of their examination:

(A) There is no reasonable expectation for improvement in the condition of the declarant; and

(B) Death of the declarant from these conditions is imminent.

GEORGIA STATUTORY SHORT FORM DURABLE POWER OF ATTORNEY FOR HEALTH CARE

NOTICE: THE PURPOSE OF THIS POWER OF ATTORNEY IS TO GIVE THE PERSON YOU DESIGNATE (YOUR AGENT) BROAD POWERS TO MAKE HEALTH CARE DECISIONS FOR YOU, INCLUDING POWER TO REQUIRE, CONSENT TO , OR WITHDRAW ANY TYPE OF PERSONAL CARE OR MEDICAL TREATMENT FOR ANY PHYSICAL OR MENTAL CONDITION AND TO ADMIT YOU TO OR DISCHARGE YOU FROM ANY HOSPITAL, HOME, OR OTHER INSTITUTION; BUT NOT INCLUDING PSYCHO SURGERY, STERILIZATION, OR INVOLUNTARY HOSPITALIZATION OR TREATMENT COVERED BY TITLE 37 OF THE OFFICIAL CODE OF GEORGIA ANNOTATED. THIS FORM DOES NOT IMPOSE A DUTY ON YOUR AGENT TO EXERCISE GRANTED POWERS; BUT, WHEN A POWER IS EXERCISED, YOUR AGENT WILL HAVE TO USE DUE CARE TO ACT FOR YOUR BENEFIT AND IN ACCORDANCE WITH THIS FORM. A COURT CAN TAKE AWAY THE POWERS OF YOUR AGENT IF IT FINDS THE AGENT IS NOT ACTING PROPERLY. YOU MAY NAME COAGENTS AND SUCCESSOR AGENTS UNDER THIS FORM, BUT YOU MAY NOT NAME A HEALTH CARE PROVIDER WHO MAY BE DIRECTLY OR INDIRECTLY INVOLVED IN RENDERING HEALTH CARE TO YOU UNDER THIS POWER. UNLESS YOU EXPRESSLY LIMIT THE DURATION OF THIS POWER IN THE MANNER PROVIDED BELOW OR UNTIL YOU REVOKE THIS POWER OR A COURT ACTING ON YOUR BEHALF TERMINATES IT, YOUR AGENT MAY EXERCISE THE POWERS GIVEN IN THE POWER THROUGHOUT YOUR LIFETIME, EVEN AFTER YOU BECOME DISABLED, INCAPACITATED, OR INCOMPETENT. THE POWERS YOU GIVE YOUR AGENT, YOUR RIGHT TO REVOKE THOSE POWERS, AND THE PENALTIES FOR VIOLATING THE LAW ARE EXPLAINED MORE FULLY IN CODE SECTIONS 31-36-6, 31-36-9, AND 31-36-10 OF THE GEORGIA "DURABLE POWER OF ATTORNEY FOR HEALTH CARE ACT" OF WHICH THIS FORM IS A PART. THAT ACT EXPRESSLY PERMITS THE USE OF ANY DIFFERENT FORM OF POWER OF ATTORNEY YOU MAY DESIRE. IF THERE IS ANYTHING ABOUT THIS FORM THAT YOU DO NOT UNDERSTAND, YOU SHOULD ASK A LAWYER TO EXPLAIN IT TO YOU.

DURABLE POWER OF ATTORNEY made this _____ day of _____ ,19___.

1. I, _____, hereby appoint
(insert name and address of principal)

_____ as my attorney in fact (my agent)
(insert name and address of agent)

to act for me and in my name in any way I could act in person to make any and all decisions for me concerning my personal care, medical treatment, hospitalization, and health care and to require, withhold, or withdraw any type of medical treatment or procedure, even though my death may ensue. My agent shall have the same access to my medical records that I have, including the right to disclose the contents to others. My agent shall also have full power to make a disposition of any part or all of my body for medical purposes, authorize an autopsy of my body, and direct the disposition of my remains.

THE ABOVE GRANT OF POWER IS INTENDED TO BE AS BROAD AS POSSIBLE SO THAT YOUR AGENT WILL HAVE AUTHORITY TO MAKE ANY DECISION YOU COULD MAKE TO OBTAIN OR TERMINATE ANY TYPE OF HEALTH CARE, INCLUDING WITHDRAWAL OF NOURISHMENT AND FLUIDS AND OTHER LIFE-SUSTAINING OR DEATH-DELAYING MEASURES, IF YOUR AGENT BELIEVES SUCH ACTION WOULD BE CONSISTENT WITH YOUR INTENT AND DESIRES. IF YOU WISH TO LIMIT THE SCOPE OF YOUR AGENT'S POWERS OR PRESCRIBE SPECIAL RULES TO LIMIT THE POWER TO MAKE AN ANATOMICAL GIFT, AUTHORIZE AUTOPSY, OR DISPOSE OF REMAINS, YOU MAY DO SO IN THE FOLLOWING PARAGRAPHS.

2. The powers granted above shall not include the following powers or shall be subject to the following rules or limitations (here you may include any specific limitations you deem appropriate, such as your own definition of when life-sustaining or death-delaying measures should be withheld; a direction to continue nourishment and fluids or other life-sustaining or death-delaying treatment in all events; or instructions to refuse any specific types of treatment that are inconsistent with your religious beliefs or unacceptable to you for any other reason, such as blood transfusion, electroconvulsive therapy, or amputation):

_____

_____

_____

_____

THE SUBJECT OF LIFE-SUSTAINING OR DEATH-DELAYING TREATMENT IS OF PARTICULAR IMPORTANCE. FOR YOUR CONVENIENCE IN DEALING WITH THAT SUBJECT, SOME GENERAL STATEMENTS CONCERNING THE WITHHOLDING OR REMOVAL OF LIFE-SUSTAINING OR DEATH-DELAYING TREATMENTS ARE SET FORTH BELOW. IF YOU AGREE WITH ONE OF THESE STATEMENTS, YOU MAY INITIAL THAT STATEMENT, BUT DO NOT INITIAL MORE THAN ONE.

I do not want my life to be prolonged nor do I want life-sustaining or death-delaying treatment to be provided or continued if my agent believes the burdens of the treatment outweigh the expected benefits. I want my agent to consider the relief of suffering, the expense involved, and the quality as well as the possible extension of my life in making decisions concerning life-sustaining or death-delaying treatment.

Initialed _____

I want my life to be prolonged and I want life-sustaining or death-delaying treatment to be provided or continued unless I am in a coma, including a persistent vegetative state, which my attending physician believes to be irreversible, in accordance with reasonable medical standards at the time of reference. If and when I have suffered such an irreversible coma, I want life-sustaining or death-delaying treatment to be withheld or discontinued.

Initialed _____

I want to be prolonged to the greatest extent possible without regard to my condition, the chances I have for recovery, or the cost of the procedures.

Initialed _____

THIS POWER OF ATTORNEY MAY BE AMENDED OR REVOKED BY YOU AT ANY TIME AND IN ANY MANNER WHILE YOU ARE ABLE TO DO SO. IN THE ABSENCE OF AN AMENDMENT OR REVOCATION, THE AUTHORITY GRANTED IN THIS POWER OF ATTORNEY WILL BECOME EFFECTIVE AT THE TIME THIS POWER IS SIGNED AND WILL CONTINUE UNTIL YOUR DEATH AND WILL CONTINUE BEYOND YOUR DEATH IF ANATOMICAL GIFT, AUTOPSY, OR DISPOSITION OF REMAINS IS AUTHORIZED, UNLESS A LIMITATION ON THE BEGINNING DATE OR DURATION IS MADE BY INITIALING AND COMPLETING EITHER OR BOTH OF THE FOLLOWING:

3. ( ) This power of attorney shall be come effective on _____ (insert a future date or event during your lifetime, such as court determination of your disability, incapacity, or incompetency, when you want this power to first take effect).

4. ( ) This power of attorney shall terminate on _____ (insert a future date or event, such as court determination of your disability, incapacity, or incompetency, when you want this power to terminate prior to your death).

IF YOU WISH TO NAME SUCCESSOR AGENTS, INSERT THE NAMES AND ADDRESSES OF SUCH SUCCESSORS IN THE FOLLOWING PARAGRAPH:

5. If any agent named by me shall die, become legally disabled, incapacitated, or incompetent, or resign, refuse to act, or be unavailable, I name the following (each to act successively in the order named) as successors to such agent:

_____

_____

IF YOU WISH TO NAME A GUARDIAN OF YOUR PERSON IN THE EVENT A COURT DECIDES THAT ONE SHOULD BE APPOINTED, YOU MAY, BUT ARE NOT REQUIRED TO, DO SO BY INSERTING THE NAME OF SUCH GUARDIAN IN THE FOLLOWING PARAGRAPH. THE COURT WILL APPOINT THE PERSON NOMINATED BY YOU IF THE COURT FINDS THAT SUCH APPOINTMENT WILL SERVE YOUR BEST INTERESTS AND WELFARE. YOU MAY, BUT ARE NOT REQUIRED TO, NOMINATE AS YOUR GUARDIAN THE SAME PERSON NAMED IN THIS FORM AS YOUR AGENT.

6. If a guardian of my person is to be appointed, I nominate the following to serve as such guardian:_____
(insert name and address of nominated guardian of the person)

7. I am fully informed as to all the contents of this form and understand the full import of this grant of powers to my agent.

Signed_____
(principal)

8. (OPTIONAL) I specifically provide that if I have executed a Living Will on or after April 16, 1992, under O.C.G.A. Chapter 32, Title 31, that the Living Will will be full force even if there continues to be an agent available to serve pursuant to this Durable Power of Attorney for Healthcare. Both the Living Will and the Durable Power of Attorney for Healthcare shall be valid except to the extent that my wishes pursuant to the Living Will are contrary to the decisions made by the agent appointed in this document, in which case the Living Will shall take precedence.

Signed_____
(principal)

The principal has had an opportunity to read the above form and has signed the above form in our presence. We, the undersigned, each being over 18 years of age, witness the principal's signature at the request and in the presence of the principal, and in the presence of each other, on the day and year above set out.

Witnesses: Addresses:

_____ _____

_____

_____ _____

_____

Additional witness required when health care agency is signed in a hospital or skilled nursing facility.

I hereby witness this health care agency and attest that I believe the principal to be of sound mind and to have made this health care agency willingly and voluntarily.

Witness: _____
(Attending Physician)

Address: _____

_____

YOU MAY, BUT ARE NOT REQUIRED TO, REQUEST YOUR AGENT AND SUCCESSOR AGENTS TO PROVIDE SPECIMEN SIGNATURES BELOW. IF YOU INCLUDE SPECIMEN SIGNATURES IN THIS POWER OF ATTORNEY, YOU MUST COMPLETE THE CERTIFICATION OPPOSITE THE SIGNATURES OF THE AGENTS.

Specimen signatures of agent and successor(s)

I certify that the signature of my agent and successor(s) is correct

_____ _____
(Agent) (Principal)

_____ _____
(Successor Agent) (Principal)

_____ _____
(Successor Agent) (Principal)

GEORGIA DEPARTMENT OF HUMAN RESOURCES
INSURANCE ASSISTANCE PROGRAM
PATIENT MEDICAL ENROLLMENT FORM

The Georgia Insurance Assistance Program continues the health insurance of HIV infected persons who are unable to work and who are not financially able to pay their monthly premium.

1. PATIENT INFORMATION

NAME_____
ADDRESS_____
TELEPHONE NUMBER_____

I hereby authorize the release of medical information pertaining to my participation in the Insurance Assistance Program to health department personnel.

SIGNATURE_____ DATE_____

2. CLINICAL INFORMATION

DIAGNOSIS: HIV Disease Date of DX_____
Most Recent T4 Count (Total) _____/mm³ Date _____

3. PHYSICIAN INFORMATION

NAME_____
ADDRESS_____
TELEPHONE NUMBER_____

SIGNATURE_____ DATE_____

Please have the patient return this completed form to the health department.

APPROVED: _____ _____
District Health Director County Health Department

_____ _____
Date Office of Infectious Disease

Georgia Department of Human Resources
Division of Public Health
Insurance Assistance Program

FINANCIAL RESOURCES

I. PATIENT INFORMATION (PLEASE TYPE OR PRINT)

NAME: Last	First	Middle	Maiden	DATE OF BIRTH ___/___/___ Mo Day Yr
RACE ☐Hispanic ☐Asian ☐White ☐Black ☐Other	SEX ☐M ☐F	MARITAL STATUS ☐Single ☐Married ☐Divorced ☐Widowed ☐Separated		PHONE
ADDRESS: Street Apt.		Zip	County	Social Security Number _____/___/_____

Georgia Resident?_____Years_____Months. Less than 6 months: Is residency permanent? ☐Yes ☐No
(Must show proof of residence, i.e. drivers license)

II. HEALTH INSURANCE COVERAGE:
Health Insurance:

☐Individual

☐Group

Currently Insured by:
Insurance Company:_____
Address: _____

_____

As documented by:

☐Statement from employer

☐Copy of latest premium bill

Georgia Department of Human Resources
Division of Family Services
Insurance Verification Section

PHYSICIAN RESPONSE

I. PATIENT INFORMATION (print or type)

Name: Last	First	Middle	Alias	Date of Birth

Sex: ☐ Male ☐ Female	Race: ☐ Black ☐ White ☐ Hispanic ☐ Asian/Pacific Islander ☐ American Indian/Eskimo ☐ Other	Height	Weight

Address: Street, Apt. No.	City	State	Zip Code

Georgia Medicaid: Yes ☐ No ☐ If yes, what type?

Treating Physician: ☐ Yes ☐ No
If no, give name of relative, i.e. mother, father

II. HEALTH INSURANCE COVERAGE:
Does Insurance:

☐ Individual

☐ Group

Currently Insured by:
Insurance Company: _____
Address:

_____

_____

_____

As documented by:

☐ Statement from employer

☐ Copy of latest premium bill

III. HOUSEHOLD MEMBERS: (Includes client, spouse, children and if client a minor, parents)

NAME	AGE	RELATIONSHIP TO PATIENT	GROSS INCOME PER MONTH	** SOURCE
1.				
2.				
3.				
4.				
5.				
6.				

(If more than 6 attach another page)

TOTAL YEARLY INCOME:** $_____ X 12 = $_____

**INCOME DOCUMENTATION: Income includes wages, rental income from apartments or boarders, child support/alimony, pensions, etc. Attach a pay check stub for last 4 weeks, most recent W-2, or notarized statement from employer verifying income. If applicable, attach statement of child support payment, Public Assistance award letter, Social Security Income award letter, Pension award letter, form from unemployment check, etc. If no income is listed, explain how living expenses are met.

CLIENT EXPENSES***	YES	NO	AMOUNT
Outstanding Medical Expenses (current)			
Anticipated Medical Expenses (per month)			
Child Support/Alimony (per month)			

***EXPENSES DOCUMENTATION: Attach a list showing the health care agency or provider, and the amount owed after insurance for outstanding medical expenses. Attach a copy of order which states amount of child support/alimony.

AGREEMENT:

I fully understand that the Insurance Assistance Program is intended only for clients with HIV infection who are unable to pay their health insurance premium. I hereby certify that the above information is complete and accurate.

_____ _____

Signature of Client, Spouse or Parent of Minor Date

_____ _____

Signature of Public Health Employee Date

_____

Health Department

I understand that the Insurance Participance Programs is intended only for clients with HIV Infection who are unable to pay their health insurance premium. I hereby certify that the above information is complete and accurate.

GEORGIA DEPARTMENT OF HUMAN RESOURCES
ANTIVIRAL DRUG THERAPY PROGRAM
PATIENT MEDICAL ENROLLMENT FORM

1. **PATIENT INFORMATION**

NAME _____
ADDRESS _____
TELEPHONE NUMBER _____

I hereby authorize the release of medical information pertaining to my participation in the Antiviral Drug Therapy Program to health department personnel.

SIGNATURE _____ DATE _____

2. **CLINICAL INFORMATION**

DIAGNOSIS: HIV Disease Date of DX _____
Most Recent T4 Count (Total) _____/mm³ Date _____

3. **PHYSICIAN INFORMATION**

NAME _____
ADDRESS _____
TELEPHONE NUMBER _____

SIGNATURE _____ DATE _____
DEA # _____

- **Prescriptions should be written for a six (6) months supply.**
- **Drugs will be mailed to patient's physician on a monthly basis.**
- **Please notify the local health department immediately if patient discontinues drug therapy on physician's advice or of his/her own accord.**
- **Please have the patient return this completed form to the health department.**

APPROVED: _____ _____
District Health Director County Health Department

_____ _____
Date Office of Infectious Disease
Slot Number

Georgia Department of Human Resources
Division of Public Health
ANTIVIRAL DRUG TREATMENT PROGRAM

FINANCIAL RESOURCES

I. PATIENT INFORMATION: (PLEASE TYPE OR PRINT)

NAME: Last	First	Middle	Maiden	DATE OF BIRTH __/__/__ Mo. Day Yr.
RACE ☐ White ☐ Black ☐ Other	SEX ☐ Male ☐ Female	MARITAL STATUS ☐ Single ☐ Married ☐ Divorced ☐ Widowed ☐ Separated		PHONE
ADDRESS: Street Apt.	City	Zip	County	Social Security Number ___/__/____

U. S CITIZEN? ☐ Yes ☐ No If No, Attach Verification of Visa.
Georgia Resident? _____ Years _____ Months. Less than 6 months: Is residency permanent? ☐ Yes ☐ No
(Must show proof of residence, i.e., drivers license)

II. INSURANCE BENEFIT PROGRAMS:
Medicaid? ☐ Yes ☐ No ☐ Pending
Medicare Part A: ☐ Yes ☐ No ☐ Pending
Part B: ☐ Yes ☐ No ☐ Pending
Private Health Insurance? ☐ Yes ☐ No If Yes, amount or % paid for antiviral drugs $ _____ / _____ %

Insurance Company: _____

Any Other Benefit Program? ☐ Yes ☐ No What? _____

III. HOUSEHOLD MEMBERS: *(Includes client, spouse, children and, if client a minor, parents)*

NAME	AGE	RELATIONSHIP TO PATIENT	GROSS INCOME PER MONTH	** SOURCE
1.				
2.				
3.				
4.				
5.				
6.				

(If more than 6 attach another page)

TOTAL YEARLY INCOME: $_____ X 12 = $_____

** **INCOME DOCUMENTATION:** Income includes wages, rental income from apartments or boarders, child support / alimony, pensions, etc. Attach a pay check stub for last 4 weeks, most recent W – 2, or notarized statement from employer verifying income. If applicable, attach statement of child support payments, Public Assistance award letter, Social Security Income award letter, Pension award letter, form from unemployment check, etc. If no income is listed, explain how living expenses are met.

APPLICATION WILL NOT BE ACCEPTED WITHOUT DOCUMENTATION

IV. CLIENT EXPENSES ***	YES	NO	AMOUNT
Out standing Medical Expenses			
Out standing Medical Expenses *(per month)*			
Child Support / Alimony *(per month)*			

*** **EXPENSES DOCUMENTATION:** Attach a list showing the health care agency or provider, and the amount owed after insurance for outstanding medical expenses. Attach a copy of Order which states amount of child support / alimony.

V. AGREEMENT:

I fully understand that the Antiviral Drug Treatment Program is intended only for clients who are unable to pay. I hereby certify that the above information is complete and accurate.

_____ _____

Signature of Client, Spouse or Parent of Minor — Date

_____ _____

Signature of Public Health Employee — Date

_____

Health Department

LAB TEST FLOWSHEET

	Base Line				
DATES					
BODY WEIGHT Your Current Weight					
WBC LEUKOCYTE COUNT White Blood Count					
POLYS					
TOTAL LYMPHOCYTE COUNT					
TOTAL T-4 CELLS Helper Inducer					
TOTAL T-8 CELLS Suppressor					
PERCENT OF T-4 CELLS					
VIRAL LOAD					
Hgb Hemoglobulin					
Hct Hematocrit					

For additional "Tracker" forms, or for help putting your test results on the chart, contact (404) 874-7926
AIDS Survival Project, 828 W. Peachtree Street, Suite 206, Atlanta, Georgia 30308

Event Tracker

Date & Time	Event Name	Description	Can you think of anything that might have brought this on?	How long did it last?
	1.			
	2.			
	3.			
	4.			
	5.			

For additional "Tracker" forms, or for help putting your test results on the chart, contact (404) 874-7926
AIDS Survival Project, 828 W. Peachtree Street, Suite 206, Atlanta, Georgia 30308

Date & Time	Event Name	Description	Can you think of anything that might have brought this on?	How long did it last?
	1.			
	2.			
	3.			
	4.			
	5.			

QUESTION LOG

Date & Time	Question	Health Care Provider's Response
	1.	
	2.	
	3.	
	4.	
	5.	

For additional "Question log" forms contact (404) 874-7926

AIDS Survival Project, 828 W. Peachtree Street, Suite 206, Atlanta, Georgia 30308

QUESTION LOG

Date & Time	Question	Health Care Provider's Response
	1.	
	2.	
	3.	
	4.	
	5.	

Medication/Treatment Tracker

Name of Medication or Treatment	Date Started	Date Stopped	Dosage / Frequency	Side Effects (if any)
1.				
2.				
3.				
4.				
5.				

For additional "Tracker" forms, or for help putting your test results on the chart, contact (404) 874-7926
AIDS Survival Project, 44 Twelfth Street, Atlanta, Georgia 30309

APPENDIX B

COMPLEMENTARY & ALTERNATIVE TREATMENT AND THERAPIES GUIDE

A listing of some of the most common alternative treatments pursued by people living with HIV Disease and AIDS. Also includes vitamins, minerals and supplements.

AIDS TREATMENT INITIATIVES

828 W. Peachtree Street, NE
Atlanta, Georgia 30308
(404) 874-4845

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Page 2	**NAC** **DHEA** **Co-Enzyme Q-10** **Ozone** **Trental**
Page 3	**Carrisyn** (acemannan) **DNCB** **Iscador** (mistletoe extract)
Page 4	**TP-5** (thymopentin) **Thymomodulin/Leucotrofina** **DTC** (imuthiol)
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Page 9-10	**Atlanta Buyers Club listing**
Page 11	**AIDS Research Consortium of Atlanta - Clinical Trials Listing**
Page 12	**University of Alabama, Birmingham ACTG Clinic 1917 - Clinical Trials Listing**

The following periodicals, treatment newsletters and medical journals were used in the compilation of this guide:

AIDS Treatment News	AmFAR AIDS/HIV Treatment Directory
PAAC Notes	The Jon Greenburg Treatment Library
Notes From The Underground	Gay Mens Health Crisis Treatment Issues
PI Perspective	Physicians Desk Reference
Bulletin of Experimental Treatment for AIDS	Journal of the MegaHealth Society
The Lancet	New England Journal of Medicine
The Journal of the American Medical Association	Monographs of Lark Lands, Ph.D.
Positively Aware	Larry M. Bruni, M.D.

Please Note:

The service of providing access to, or information about, treatments or therapies in no way implies a recommendation, endorsement, or any claim of treatment efficacy. The staff at ABC are not licensed medical professionals. We strongly encourage you to discuss all treatment options and strategies with your primary health care providers.

COMPLEMENTARY & ALTERNATIVE HIV/AIDS THERAPIES

Treatment Name/Function	Research Results	Comments	Possible Adverse Effects
Compound Q - (Trichosanthin) *extract of Chinese cucumber root* **Anti-Viral**	• T-4 cell increases • Dr. Waites found:[1] -dramatic T-4 cell increases in 8-10% -stable T-4 counts in many others • Dr. Gorelick found:[2] -dose related increases in total number of T-cells, both CD-4 & CD-8	•In clinical Trials •Availability: - some Buyers Clubs - direct from China •Dose: variable	•Allergic reaction; possible anaphylactic shock; possible increased intracranial pressure; flu-like symptoms, muscle aches, headache, fevers, temporary decreased immunity, fluid retention
Glycyrrhizin *licorice root extract* **Anti-Viral**	• In vitro: - Inhibits HIV replication - Interrupts virus-to-cell binding - Inactivates herpes - Decreases syncytia • In vivo: - For 1-2 years, 10 patients on IV glycyrrhizin (150-225 mg/day) had no disease progression, while 3 of 10 in control group did.[3] - In 5 using IV glycyrrhizin (400-1600mg/day) had reduced P-24 antigen levels, 3 went P-24 negative.[4] • Anecdotal Reports: - Reversed decline of CD-4 cell counts - Normalized liver enzymes - Improved well being	•Availability: - some Buyers Clubs - Japan-over the counter. •Dose:400-500 mg per day (anecdotal)	•Fluid and soduim retention •Potassium loss •Muscle soreness •Fatigue •Elevated blood pressure
Hypericin *western herb* **Anti-Viral**	• In vitro: - prevents infection of new cells - may work synergistically with AZT • In vivo: - At lower doses, several trials have found no significant clinical improvement or have ended before results were obtained. At higher doses, using synthetic Hypericin, trials were discontinued due to increased photosensitivity.[5]	•Availability: - food & vitamin stores - most U.S. Buyers Clubs •Dose 10-40 mg/day	•Increased sensitivity to sunlight at higher doses •Liver toxicity-check liver levels regularly •Anti-depressant: do not take with other MAO inhibitors

COMPLEMENTARY & ALTERNATIVE HIV/AIDS THERAPIES

Treatment Name/Function	Research Results	Comments	Possible Adverse Effects
NAC-(N-acetylcysteine) *form of amino acid cysteine* **Anti-Viral**	• In vitro: - reduced viral replication up to 90 % - decreased HIV Protein synthesis • In vivo: - decreased P-24 antigen levles[6] - Dr. Montagnier found decreased apoptosis of T-cells for 15 patients on 1200mg/day[7] - increased glutathione levels[8] - decreased TNF levels[9] • Anecdotal Reports: - increased energy levels	•Available Buyers Clubs •Vitamin Stores •Canadian clinical trials for use in Bactrim desensitization protocol •Dose 1000-2000 mg day	•Possible upset stomach or diarrhea •No other reported toxicity
DHEA-*(*dehydropiandrosterone*)* *precursor to the hormone testosterone* **Anti-Viral**	• In vitro: - DHEA level is decreased early in HIV infection and for people with full blown AIDS - moderate selective inhibitory effect on HIV replication	•Available some US Buyers Clubs •Available in Europe •Dose 50-1000mg/day	•Antagonistic to AZT •Causes the release of testosterone •No side effects have been reported
Co-Enzyme Q-10-(Ubiquinone) *combination of herbs* **Anti-Viral**	• Important in supplying energy to cells • Crucial for thymic activity • In conjunction with AZT, it may decrease muscle necrosis	•Available most US Buyers Clubs & vitamin stores •Dose: 10-30mg, 3 times/day	•No reported toxicities or adverse interactions
Ozone **Anti-Viral**	• Anecdotal Reports: - Increase in T-cell counts - Decreased P-24 antigen - Decreased symptoms - Many report no benefit	•Dose: taken rectally or by infusion using ozone generator	•Non-toxic if not inhaled
Trental(Pentoxifylline) **Anti-Viral**	• 11 of 13 studied had TNF levels drop & decrease in triglycerides.[10] • Five studied had an HIV-titer drop.[10] • Enhances ddI's anti-viral activity[11]	•FDA approved for treatment of leg cramps •Trials in Boston & New York •Available by Rx. •Dose:400mg 3x/day	•Low toxicities found. •One study patient had recurrent fevers •May mask signs of infection

COMPLEMENTARY & ALTERNATIVE HIV/AIDS THERAPIES

Treatment Name/Function	Research Results	Comments	Possible Adverse Effects
Carrisyn-(Acemannan) **Immune Modulator**	• In one study, patients had an initial T-4 count of 340, after six months 450, and after one year 613.[12] • Symptom improvement; no toxic side effects. • Synergistic with AZT[13] • Stimulates macrophages to release interleukin-1 and interferon, which signals the immune cascade (proteins which activate the immune response[14] • Interferes with HIV's ability to replicate in infected cells[15]	•Carrington Labs makes Acemannan in injectable and oral forms.	•Diarrhea •Irritates the digestive tract •No reported toxicity
DNCB-(DiNitroChloroBenzene) **Immune Modulator**	• In study with 20 patients, stable CD-4 counts, significant increases in T-8 and NK cells, and decreased HIV replication.[16] • In study of long-term DNCB users, 24 had decreased viral load (measured by RT-PCR) and viral activity, and increased CD-8 counts.[17]	•No trials •Extensively used on west coast •Dose: periodic topical applications •De-sensitization necessary •Available Healing Alternatives-SF	•Localized temporary, itchy rash •No reported toxicity
Iscador *mistletoe extract* **Immune Modulator**	• In vivo: - Increased T-4/T-8 ratios in women with breast cancer[18] • Anecdotal: (Dr. Marti)[19] - Increased T-4 cells, interferon, NK cells, antibody response, lymphocytes • May reduce bone marrow suppression from AZT • May decrease viral replication	•European Trials •Available by Rx. Institut Hischia in Switzerland •Dose: Subcutaneous injection, 2x's/week Dose escalate from .01mg to 10-20mg Maintenance at 20mg 3X's/week	•Painful welts at injection site •Liver toxicity

COMPLEMENTARY & ALTERNATIVE HIV/AIDS THERAPIES

Treatment Name/Function	Research Results	Comments	Possible Adverse Effects
TP-5-(Thymopentin) **Immune Modulator**	• In Italy, 41 subjects, TP-5 has shown significant increase in T-4 cells and decrease in symptoms[20] • In S.F. & Cleveland, 47 on TP-5 & 44 placebo, with TP-5 no one progressed to ARC/AIDS,P-24 levels remained stable, all maintained T-4 cell counts, in 25% Beta-2 levels decreased to normal.[21] • Dr. Marcus Conant's initial trial found stablized CD-4 counts and significantly less disease progression[22]	•Few U.S. trials •Johnson & Johnson may start expanded access soon •Available by Rx. in Italy •Dose: 50mg 3X's/wk by subcutaneous injection	•No adverse effects noted in current research
Thymomodulin / Leucotrofina *calf thymus* **Immune Modulator**	• In one study, increased T-4 cells and reduced T-8 cells in patients without full blown AIDS.[23] • Normalizing CD-4/CD-8 ratio. • Improved clinical symptoms.	•Available by Rx. from Italy. •Dose: Loading: one 60mg capsule in a.m. on empty stomach for 14 days Maintenance: one 60mg. capsule every other day.	• Initial immune suppression response. Must be taken with an anti-viral.
DTC-(Imuthiol) Levamisole *{Levamisole was initially found to boost the immune system in dogs. DTC was formulated as a copy of Levamisole, to bypass patent restrictions.}* **Immune Modulator**	• Contradictory results over the past six years. Some trials have shown it to be useful, others have useless, even harmful. • Positive results include that intravenously, it has been found to delay disease progression and stabilize T4 cell counts, as well as to improve symptoms. Studies showed clearance of CMV and herpes zoster. • A study in France showed that people on DTC did better than those on placebo the first year, but after two years the disease progressed more rapidly. This may support the theory that HIV overactivates the immune system.[24]	•Dose: DTC-500mg/wk. Levamisole-50 to 100mg 2X's/wk consecutive days •Availability: DTC by Rx. from New Zealand Levamisole at some US Buyers Clubs	•Minor stomach cramps and/or nausea. •Sensory stimulation. •Decreased Neutrophils. •Elevated liver enzymes. •Avoid **all** alcohol 24 hours before and 48 hours after taking.

COMPLEMENTARY & ALTERNATIVE HIV/AIDS THERAPIES

Treatment Name/Function	Research Results	Comments	Possible Adverse Effects
TP-5-(Thymopentin) **Immune Modulator**	• In Italy, 41 subjects, TP-5 has shown significant increase in T-4 cells and decrease in symptoms[20] • In S.F. & Cleveland, 47 on TP-5 & 44 placebo, with TP-5 no one progressed to ARC/AIDS,P-24 levels remained stable, all maintained T-4 cell counts, in 25% Beta-2 levels decreased to normal.[21] • Dr. Marcus Conant's initial trial found stablized CD-4 counts and significantly less disease progression[22]	•Few U.S. trials •Johnson & Johnson may start expanded access soon •Available by Rx. in Italy •Dose: 50mg 3X's/ wk by subcutaneous injection	•No adverse effects noted in current research
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DTC-(Imuthiol) Levamisole *[Levamisole was initially found to boost the immune system in dogs. DTC was formulated as a copy of Levamisole, to bypass patent restrictions.]* **Immune Modulator**	• Contradictory results over the past six years. Some trials have shown it to be useful, others have useless, even harmful. • Positive results include that intravenously, it has been found to delay disease progression and stabilize T4 cell counts, as well as to improve symptoms. Studies showed clearance of CMV and herpes zoster. • A study in France showed that people on DTC did better than those on placebo the first year, but after two years the disease progressed more rapidly. This may support the theory that HIV overactivates the immune system.[24]	•Dose: DTC-500mg/wk. Levamisole-50 to 100mg 2X's/wk consecutive days •Availability: DTC by Rx. from New Zealand Levamisole at some US Buyers Clubs	•Minor stomach cramps and/or nausea. •Sensory stimulation. •Decreased Neutrophils. •Elevated liver enzymes. •Avoid **all** alcohol 24 hours before and 48 hours after taking.

REFERENCES

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VITAMINS & OTHER SUPPLEMENTS

Source: *Journal of MegaHealth Society*, June '90

Name	Research Results/Rationale	Possible Adverse Effects
Vitamin A & βCarotene	Essential for T and B cell production. Protects against cancer. Increases cellular immunity and antibody activity. Accelerates production of various disease-fighting cells. Maintains protection barriers against infectious organisms. Produces bacteria fighting lysosomes. Supplementation may enhance immune response.	Vitamin A: headache, nausea, vomiting, diarrhea, decreased appetite, weight loss, joint pain βCarotene: None
Vitamin B_1	Deficiency decreases thymus gland integrity, antibody response, resistance to infections, total number of T and B cells	toxic in high hypodermic doses
Vitamin B_2	Deficiency decreases antibody response, total number of T and B cells, and spleen cell response.	toxic in high hypodermic doses
Vitamin B_3	Decreases free fatty acids, triglycerides and cholesterol in the blood. Excessive levels of these blood lipids depress immunity. A powerful releaser of growth hormone that stimulates immunity.	
Vitamin B_5	Deficiency decreases antibody response and cellular immunity. Necessary for antibodies release from plasma cells, spleen reactions and immunoglobulin responses. Inhibits tumors.	
Vitamin B_6	Most important B vitamin for normal immune functioning. Helps maintain cell and humoral mediated immune reactions. Necessary for antibody formation, T and B cell numbers, spleen response and phagocytosis. Deficiency produces profound immune impairments.	Very toxic in high hypodermic doses, neurological damage
Vitamin B_{12}	Essential to produce immune cells and fight bacteria. Exerts regulatory influence on T cells. Deficiency decreases blood cell phagocytosis and lymphocyte activity.	No toxicity symptoms known
Vitamin C	Inactivates viruses. Enhances neutrophils. Increases interferon and thymic reactions. Counteracts immuno-suppression by corticosteriods released from the adrenal glands during stress. Antihistamine effect decreases suffering from allergies. Is an antioxidant that protects phagocytic cells like neutrophils against releasing toxic oxidants, counteracts tissue inflammation and inhibits oxidative stress damage. Supplementation may improve immune competence.	Nausea, rash, abdominal cramps, diarrhea, kidney stones, hemolysis, fatigue, interferes with copper absorption.
Vitamin D	Regulates B cells and helper T cells. Deficiency lowers response to antigens.	Excess D supplementation suppresses immunity, decreases interleukin II of white blood cells.
Vitamin E	Necessary for T and B cell production and white blood cell functions. Protects phagocytes and prostaglandins. Prevents oxidative and inflammatory tissue damage. Supplementation may increase resistance to infections and cell phagocytosis. Makes T-cells react faster and more strongly. Stimulates antibody production.	gastrointestinal discomfort, fatigue, slowed blood clotting

VITAMINS & OTHER SUPPLEMENTS

Source: *Journal of MegaHealth Society*, June '90

Name	Research Results/Rationale	Possible Adverse Effects/Toxicity
Biotin	Necessary for primary and secondary antibody responses	No toxicity symptoms known.
Chromium	Prevents metabolic immunosupppression by activating insulin to prevent over secretion of insulin. Controls blood glucose levels and improves glucose tolerance.	
Copper	Necessary for antibody response, infection resistance and cell mediated immunity.	Rare neurological damage.
Folic Acid	Protects against immune tissue damage. Necessary for cellular and humoral immunity. Maintains T to B cell ratios. Deficiency lowers immunoglobulin response and blood cell phagocytosis.	Toxic in large doses. May damage kidneys. Decreased zinc availability
Iodine	Necessary for leukocyte activity.	
Iron	Deficiency impairs neutrophils and lymphoctye responses.	Liver toxicity, infections, constipation
Manganese	Stimulates natural killer cells and antibody activity	
Magnesium	Necessary for immunoglobulin reactions and resistance, infections and humoral immune responses.	Thirst, drowsiness, damaged nerves, disturbs Ca/Mg balance.
Selenium	Increases natural killer cells, immunoglobulins and antibody production. Increases phagocytic cell activity. Protects macrophages against free radical destruction. Helps protect against cancer. Prevents inflammation and oxidative damage.	Weakness, pancreas damage, heart disease, brittle hair and nails, fatigue, nausea, dizziness, diarrhea.
Zinc	Increases natural killer cells, cell mediated immunity and phagocytosis. Strengthens macrophages. Essential for the health of the thymus gland and lymph nodes.	Nausea, vomiting, diarrhea, dizziness, impaired smell and taste, interference with calcium, copper and iron absorption.

Additional Vitamin/Supplement Information

Dr. Richard Beach and associates at the University of Miami School of Medicine noted widespread nutrient deficiency among 108 men with CD4 cell counts between 200 and 700[1]. Based on the findings, researchers made dietary recommendations for these vitamins and nutrients expressed in terms of the United States Recommended Dietary Allowance (USRDA):

1. Beach, R., et. al. *Interim dietary recommendations to maintain adequate blood nutrient levels in early HIV-1 infection.* VIIIth International Conference on AIDS #PoB3675 Amsterdam, July 1992

Study Suggested RDA

A	10 times USRDA
B2	6 times USRDA
B6	10 times USRDA
B12	25 times USRDA
C	6 times USRDA
E	6 times USRDA
Zinc	5 times USRDA

PRODUCTS ACCESSIBLE THROUGH AIDS TREATMENT INITIATIVES

Name	Research Results/Rationale	Possible Adverse Effects	Requirements
Acidophilus	Helps prevent candidiasis overgrowth and digestive malfunction.	None reported. Take with meals.	None
Ampho-B Lozenges	Amphotericin-B throat lozenges, 10mg. for treatment of chronic, recurrent, non-responsive thrush.	Use under physician supervision. Could become resistant to Ampho-B.	Physician Prescription
B-12 Nasal Gel	Helps with fatigue and some neuropathy. Essential to produce immune cells and fight bacteria. Exerts regulatory influence on T cells. Deficiency decreases blood cell phagocytosis and lymphocyte activity.	No toxicity symptoms known	None
Beta Carotene	Major anti-oxidant. May increase low CD-4 cell counts.	None reported even at high dose.	None
Co-Enzyme Q-10	Important in supplying energy to cells. Important for thymic activity and therefore T-cell formation and functioning. Recommended if using AZT, it may decrease muscle necrosis.	FDA Phase I trials reveal no toxicity at any dose level.	None
Curcumin	May inhibit the *long terminal repeat* (LTR) sequence of HIV. **AIDS Treatment News** reported the LTR of HIV appears to be critically important in "turning on" the virus, suggesting that inhibiting the LTR could slow or stop virus which has already been activated. (*AIDS Treatment News* Issue 176, p.1)	Extremely large doses caused stomach ulcers in lab rats.	None
d4T (Stavudine)	Nucleoside analog. Stops reverse transcriptase production, inhibiting HIV replication. No effect on cells already infected with HIV. Less toxicity and higher quality of life, than with some other nucleoside analogues, reported by many. Is also available from Bristol-Meyers Squibb through the parallel track program. Consult your physician for further information.	In high doses some reports of neuropathy and pancreatitis.	Patient Monitoring Form signed by a licensed physician.
Derma Heal	A natural skin protectant that contains no drugs or steroids. Beneficial results have been achieved by many people suffering from foliculitis, itchy red bump syndrome, and dry flaky skin.	No adverse effects reported.	None
DHEA	Precursor to the male hormone testosterone. A moderate selective inhibitory effect on HIV replication, also antagonistic to AZT. Causes the release of testosterone and cortisol. May improve T-cell performance. DHEA has been associated in medical literature with a modest inhibition of HIV and EBV, and enhanced interleukin-2 synthesis by activated T-cells.[1]	No adverse effects reported.	Signed Informed Consent Form
L-Carnitine	Amino acid compound currently in clinical trials at NIH for its effects on myopathy (muscle weakness and/or pain and/or fatigue) which may be either HIV or AZT related.	No adverse effects reported.	None
Leucotrofina	Induces maturation of T-cells, restores antibody response and circulating leukocytes. Increases production of thymic hormones.	Initially immunosuppressant, must be used in conjunction with an antiviral.	Physician Prescription
NAC	Induces the body to increase glutathione (needed for energy generation, DNA synthesis and other cell functions, protects cells against oxidizing agents and may play a role in inhibiting HIV replication). NAC has a decreasing effect on Tumor Necrosis Factor (TNF). Elevated levels of TNF are believed to enhance HIV replication, can cause wasting syndrome, and have been associated with HIV disease progression. TNF can cause a generalized	Small percentage of individuals may experience stomach discomfort at high doses. Generally counteracted when taken with food.	None

1. **AIDS Treatment News** Issue #150, p.7

PRODUCTS ACCESSIBLE THROUGH AIDS TREATMENT INITIATIVES

Name	Research Results/Rationale	Possible Adverse Effects	Requirements
NAC	inflammatory response, possibly dysregulating the immune system. NAC is also in trials in Canada for use in a Bactrim desensitization protocol. Results from this trial were encouraging enough to open it up to a multi-center trial.		
Jarrow Pak+	A specialized formulation of selected Chinese herbs, minerals and vitamins to be used as a daily dietary supplement.	Take with food. May cause gastric distress on an empty stomach.	None
PCM-4	A combination of Siberian ginseng and porcine spleen peptide extract. Researchers have found the Siberian ginseng stimulated the activity of T-helper (CD4) cells and T-killer (CD8) cells. The polypeptides are claimed to increase well-being, B and T-cell activity, and total serum protein.	No adverse effects reported.	None
Pentamidine	FDA approved prophylaxis against pneumocystis carinii pneumonia for those who are intolerant or allergic to the sulfa based drugs bactrim and dapsone.	Cough, bronchospasm, fatigue, metallic taste, shortness of breath, decreased appetite, dizziness, rash, nausea, night sweats, chills and vomiting.	Physician Prescription
Peptide-T	Designed to block HIV/gp120 receptor binding and thereby decrease infectivity of new cells by HIV. Neural messenger. Significant improvements in memory, cognition, learning and motor skills. Stable T-4 cell counts. Currently in clinical trials to determine benefits fighting neuro-psychological effects of HIV infection (dementia and neuropathy).	None reported even at extremely high doses.	None
Resist!	A combination of selected Chinese herbs and roots, intended to be used as part of a daily dietary supplement.	No adverse effects reported.	None
Sporanox	FDA approved as an antifungal. Generally used in individuals who do not respond well to fluconazole. Effective in treating chronic vaginal yeast infections.	Do not combine with Seldane. May cause elevated liver functions. Liver enzymes must be monitored regularly.	Physician Prescription
St. Johnswort	In vitro, prevents new cell infection. May reduce symptoms. May work synergistically with AZT.	At extremely high doses, may cause sensitivity to sunlight; liver toxicity. If more than 10mg/day used, check liver enzymes regularly.	None
Vitamin C (*buffered/powdered*)	In vitro, showed decreased viral activity including reduced levels of P-24 antigen, decreased syncytia formation, decreased reverse transcriptase. Best if taken throughout the day. May be synergistic with B-12.	At extremely high doses, nausea, cramps, diarrhea. May need to build up tolerence over a long period.	None
Vitamin E	Anti-oxidant. Found to potentiate AZT.	None reported.	None
Viroterm	Sublingual low dose alpha interferon (200 I.U.). Some report increases in T-4 counts and benefits in treating external Kaposi's sarcoma. The NIH may be initiating trials in early to mid 1994 through the CPCRA network.	No adverse effects reported.	Signed Informed Consent Form

This listing represents products currently accessible through the Atlanta Buyers Club (ABC). As new treatments and therapies are identified, we thoroughly investigate them for efficacy and provide access to those that show promise and are safe for human use. Pharmaceutical grade products and those that may have potential adverse effects, require close monitoring by a licensed physician. For an updated listing of products available, please contact ABC at the address or phone number listed below.